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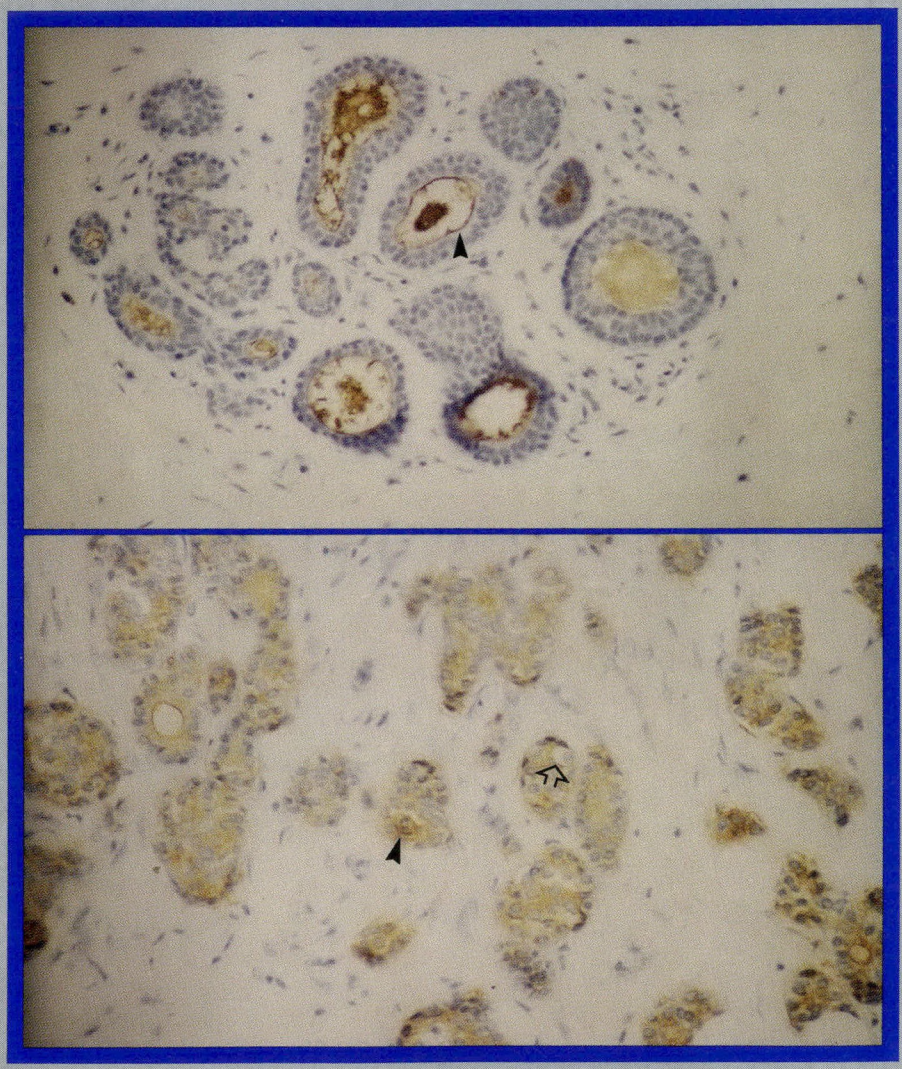
Le journal canadien de chirurgie

Vol. 34, No. 1 February 1991 février



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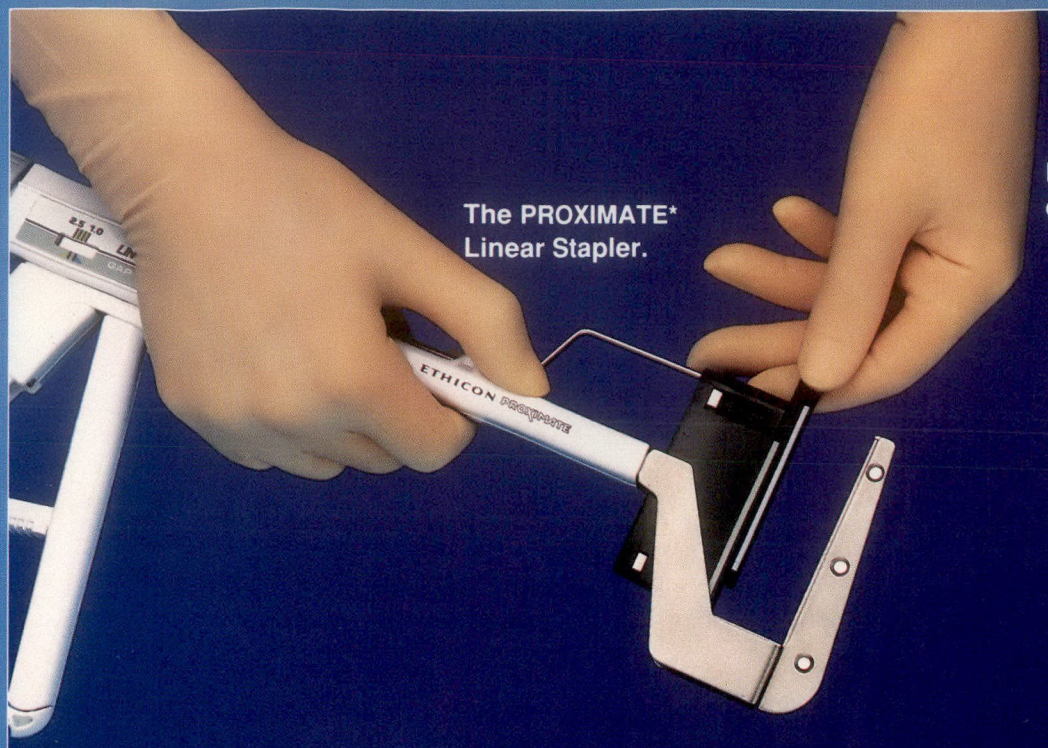

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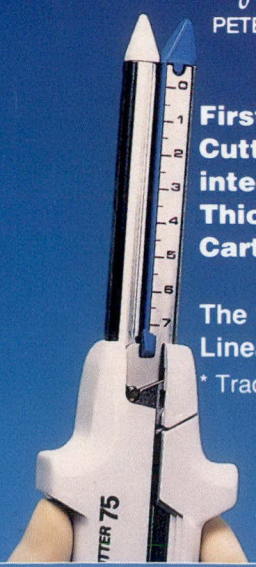

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Cover picture

Staining of benign (top) and malignant (bottom) breast tissue with the monoclonal antibody LICR-LON-M8. The use of this immunohistochemical technique as a possible method for identifying micrometastases of breast cancer is reported on pages 15 to 19.

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References:
1. Professional Studies Limited, Market Research Study, October 1990.
2. Shankardass K, et al.: Bowel function of long-term tube-fed patients consuming formulae with and without dietary fiber. JPEN, 14: 5; 508-512, 1990.

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Detailed instructions to contributors, in English and French, appear on pages 79 and 80 of the February 1991 issue.

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On trouvera des renseignements détaillés aux contributeurs, en anglais et en français, aux pages 79 et 80 de la livraison de février 1991.

Nonoperative Management for Adults With Blunt Splenic Trauma

W.J. Temple, MD, FACS, FRCSC

Director of surgery, Tom Baker Cancer Centre, Calgary. Member, Editorial Board, Canadian Journal of Surgery

In this issue (pages 27 to 29) Stephen and colleagues show that, by clinical assessment, some patients with lacerated spleens from blunt trauma may be managed safely without laparotomy. It is evident that these patients were a very select group. In the nonoperative group, 24% of the patients presented with delayed signs and symptoms, blood transfusion requirements were less and a peritoneal tap was not performed. All these features were in sharp contrast to those in the surgically managed group. The findings of Stephen and colleagues support those of a similar, retrospective study done in our centre.[1]

However, this conservative approach, as indicated by Stephen and colleagues, is fraught with hazards if strict criteria are not adhered to. I would like to re-emphasize them, because, in our centre over the last few years, inappropriate application of these principles has resulted in patients suffering substantial morbidity.

The criteria that I believe should be applied for nonoperative management of adults with blunt splenic trauma are as follows:

- Minimal abdominal signs, isolated to the left upper quadrant.
- A negative abdominal tap, if performed.
- A clinically stable patient requiring less than 2 units of blood to stabilize blood pressure and maintain vital signs.
- A splenic or perisplenic lesion documented radiologically.

In making a decision to use a nonoperative approach, the surgeon must carefully weigh the risks and benefits of observation for a documented splenic injury. The risk of overwhelming sepsis after splenectomy is lower in adults than in children but is still of some concern. When surgery is delayed after conservative management has failed, a much lower splenic salvage rate and higher transfusion requirements have been reported.[2] Transfusion of more than 2 units of blood is associated with as much morbidity from the risk of hepatitis as is the potential for overwhelming pneumococcal sepsis if splenectomy is performed. Rebleeding after discharge in patients treated conservatively has not been documented, but this risk appears to be negligible.

The potential morbidity of conservative management must be weighed against the dramatic improvements in splenorrhaphy, which can be performed successfully in 88% of grades I and II and in 60% of grade III splenic injuries, found in the majority of patients suitable for a conservative approach.[3] My own modification of the Dexon-mesh wrap technique salvaged the spleen in six consecutive patients with grade III or IV splenic injuries. This technique has controlled blood loss quickly without subsequent rebleeding. It is best described as a compression splenorrhaphy. The technique is as follows: The spleen is mobilized rapidly into the midline from its peritoneal and retroperitoneal attachments, as in a standard splenectomy. A vascular clamp may be applied across the pedicle for a few minutes. The clamp, which immediately stops the bleeding and gives the surgeon time to work on the spleen, is removed as soon as possible. A piece of Dexon mesh is used to wrap the entire spleen, leaving a small opening for the pedicle in the following manner. The mesh is cut half-way along one side to the centre. The pedicle is placed at the centre of the mesh. The short gastric vessels may be ligated to decrease the width of the pedicle. The cut in the mesh is then closed with a running suture, starting snugly at the pedicle and progressing to the edge of the mesh. Malitene may be applied over the bleeding areas or placed into the laceration to assist hemostasis. The mesh is then wrapped over the spleen, as one would wrap a gift, and the excess

trimmed. A running suture is used to close the mesh, making it into a bag. The key to success is to decrease the size of the mesh bag progressively with running sutures until the spleen is compressed enough that the bleeding stops. This may result in the spleen being smaller than its original size but is likely a temporary condition.

This compression technique is quick and effective, taking only 10 to 15 minutes, and is a dependable alternative for any patient with splenic injury not fulfilling the criteria for conservative management. The preliminary results of this technique are so impressive that it will likely prove useful in avoiding splenectomy in some patients, even when there is associated splenic damage and multiple intra-abdominal injuries.

Stephen and his colleagues are to be congratulated for bringing this subject once more to our attention.

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3. FELICIANO DV, BITONDO CG, MATTOX KL et al: A four-year experience with splenectomy versus splenorrhaphy. *Ann Surg* 1985; 201: 568–574

BOOKS RECEIVED

This list is an acknowledgement of books received. It does not preclude review at a later date.

Aids and the Lung. Edited by David Mitchell and Ashley Woodcock. 109 pp. Illust. *British Medical Journal*, London. 1990. £10. ISBN 0-7279-0289-X. Articles reprinted from *Thorax*. Available from American College of Physicians, PO Box 7777-R-0270, Philadelphia, PA 19175

Atlas of Surgery of the Liver, Pancreas and Biliary Tract. Kenneth W. Warren, Roger L. Jenkins and Glenn D. Steele Jr. 420 pp. Illust. Appleton & Lange, East Norwalk, Conn. 1991. $145. ISBN 0-8385-0128-1

The Breast. Edited by Kirby I. Bland and Edward M. Copeland III. 1128 pp. Illust. W.B. Saunders Company/Harcourt Brace Jovanovich, Inc., Philadelphia. 1991. Price not stated. ISBN 0-7216-2234-8

Clinical Anesthesia in Neurosurgery. 2nd ed. Edited by Elizabeth A.M. Frost. 593 pp. Illust. Butterworth-Heinemann, Boston. 1991. $98 (US). ISBN 0-409-90171-7

A Color Atlas of Endovascular Surgery. Rodney A. White and Geoffrey H. White. 157 pp. Illust. J.B. Lippincott Company, Philadelphia. 1990. $129.50 (US). ISBN 0-397-58328-1

Cryosurgical Treatment for Skin Cancer. Emanuel G. Kuflik and Andrew A. Gage. 266 pp. Illust. Igaku-Shoin Medical Publishers, Inc., New York. 1990. Price not stated. ISBN 0-89640-157-X

Diagnostic Techniques in Urology.. Edited by Patrick H. O'Reilly, Nicholas J.R. George and Robert M. Weiss. 617 pp. Illust. W.B. Saunders Company, London/Harcourt Brace Jovanovich, Inc., Philadelphia; HBJ-Holt-Saunders Distribution Services, Toronto. 1990. Price not stated. ISBN 0-7216-3116-9

The History of Endocrine Surgery. Richard B. Welbourn. 409 pp. Praeger, New York. 1990. $75 (US). ISBN 0-275-92586-2

Intracranial Vascular Malformations. American Association of Neurological Surgeons Publications Committee, Daniel L. Barrow. Neurosurgical Topics series. 250 pp. Illust. American Association of Neurological Surgeons, Park Ridge, Ill. 1990. AANS members, $70, nonmembers, $80, residents, $60 (add $10 outside US). ISBN 0-9624246-6-8

Laparoscopy for Surgeons. Barry A. Salky. 157 pp. Illust. Igaku-Shoin, New York. 1990. Price not stated. ISBN 0-89640-166-9

Lasers in Otolaryngology-Head and Neck Surgery. Edited by R. Kim Davis. 208 pp. Illust. W.B. Saunders/Harcourt Brace Jovanovich, Inc., Philadelphia. 1990. Price not stated. ISBN 0-7216-3124-X

The Lumbar Spine. The International Society for the Study of the Lumbar Spine. Editorial Committee, James N. Weinstein and Sam W. Wiesel. 1035 pp. Illust. W.B. Saunders Company, London/Harcourt Brace Jovanovich, Inc., Philadelphia; HBJ-Holt-Saunders Distribution Services, Toronto. 1990. Price not stated. ISBN 0-7216-9337-7

Oral and Maxillofacial Trauma Volumes 1 and 2. Edited by Raymond J. Fonseca and Robert V. Walker. 1252 pp. Illust. W.B. Saunders/Harcourt Brace Jovanovich, Inc., Philadelphia. 1991. Price not stated. ISBN 0-7216-2568-1

Orthopaedics in Infancy and Childhood. 2nd ed. G.C. Lloyd-Roberts and J.A. Fixsen. 226 pp. Illust. Butterworth-Heinemann, Boston. 1990. $150 (US). ISBN 0-7506-1030-1

Pediatric Urology. Keith W. Ashcraft. 540 pp. Illust. W.B. Saunders/Harcourt Brace Jovanovich, Inc., Philadelphia. 1990. Price not stated. ISBN 0-7216-2746-3

Surgery of the Thyroid and Parathyroid Glands. 3rd ed. Blake Cady and Ricardo L. Rossi. 348 pp. Illust. W.B. Saunders Company/Harcourt Brace Jovanovich, Inc., Philadelphia. 1991. Price not stated. ISBN 0-7216-3462-1

Surgical Oncology. Edited by C.S. McArdle. 332 pp. Illust. Butterworths, London. 1990. $165 (US). ISBN 0-407-01700-3

Fear of Flying and Surgery

Nelson S. Mitchell, MD, FRCSC

Department of Surgery, Royal Victoria Hospital, Montreal

As a schoolboy during World War II, I was obsessed with aircraft and flying. Spitfires, Hurricanes, Me 109s and 110s, drawn in various configurations of flight, took up every available space in my school books. I built and flew — or more often crashed — countless balsa models.

About the time I began training in surgery I learned that I was afraid of flying. Trips to meetings or courses in Toronto, Chicago or points distant, presented great logistical problems . . . how to avoid the jet and travel on the ground.

At the beginning of my surgical practice a surgical acquaintance took me flying in his two-seater Super-Cub. As I sat behind him, unable to protest, we flew under a bridge in the Halifax harbour. Fortunately this act of wanton foolishness was followed by a ride in a float plane where the great safety of flight was emphasized. I began flying lessons shortly thereafter. Pilot licence, night flying and instrument ratings and the purchase of an aircraft soon followed. Eighteen years later I have spent 1500 hours flying all over North America and five times that time in the operating room. I have found that much of pilot training has implications for the surgeon.

Before each flight the charts, the weather at departure, en route and at the destination must be evaluated for an expeditious and safe trip. The surgical approach must also be planned with knowledge of anatomical charts, taking into account the objective of surgery, possible deviations and obstacles that might arise. If the weather at the destination is marginal an alternative aerodrome must be selected . . . . Will the patient need to be transferred to the intensive care unit postoperatively? Is a bed available?

Before starting the engine(s) the pilot must be completely familiar with the equipment he is using. He walks around the aircraft inspecting it and its systems. In the cockpit, further static and operational checks are made according to a prearranged plan. A complete understanding of the structure and functions of the patient is taken for granted, but how many of us ensure that we have done so with a check list? How many operations have been delayed or the result compromised by faulty or absent equipment, which a preoperative check might have turned up?

During the taxi and take-off phase, while the flight can still be aborted, further regimented system checks are made. Aloft the pilot continuously monitors his engine and system instruments and his progress. He constantly contemplates what could go wrong with machine or weather and how he would deal with it. The surgeon, likewise, should continuously consider if the procedure is going according to plan. As the dissection proceeds he should look for danger signals and contemplate what complications might occur and how best to avoid them. Is there a danger of entering bowel or a vessel? How can the risk be minimized and what to do if the dreaded event occurs?

As prelanding checks are read off on the approach to the airport, so the end of the operation is a time to review postoperative orders and rehabilitation plans. Upon landing a debriefing is carried out and points of interest are recorded in the log. How often does the surgeon discuss with the operating team the conduct of a operation with a view to improving performance?

In all of the above my pilot training was the most useful to me in risk management and damage control. The surgeon can avoid most intraoperative complications by anticipating them, but when they arise, panic can be avoided by having a predetermined plan. Even in its absence, the conviction ingrained during training that virtually every problem is solvable will stand both pilot and surgeon in good stead.

I am mildly apprehensive during every flight. I have been truly frightened only twice, both times because of unfamiliarity with a system or failure of planning. I have had two engine failures, but these were without consequence as contingency plans were available and were used. Early in my pilot training, before these responses were developed, I wrecked an aircraft.

The operating room has always been a place in which I am somewhat frightened. When complications arose I had to train myself to remain calm. Anticipation and contingency planning has reduced these to rare occurrences. Those surgeons who disclaim any fear in the operating room are likely to have at least some "incidents" during their careers: the Department of Transport calls a wreck without injury an incident, reserving "accident" for a worse occurrence.■

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1. Lundstrom V. Treatment of primary dysmenorrhea with prostaglandin synthetase inhibitors—A promising therapeutic alternative. Acta Obstet Gynecol Scand 1978; 57:421-428.
2. Compendium of Pharmaceuticals and Specialties. 25th Edition, 1990.

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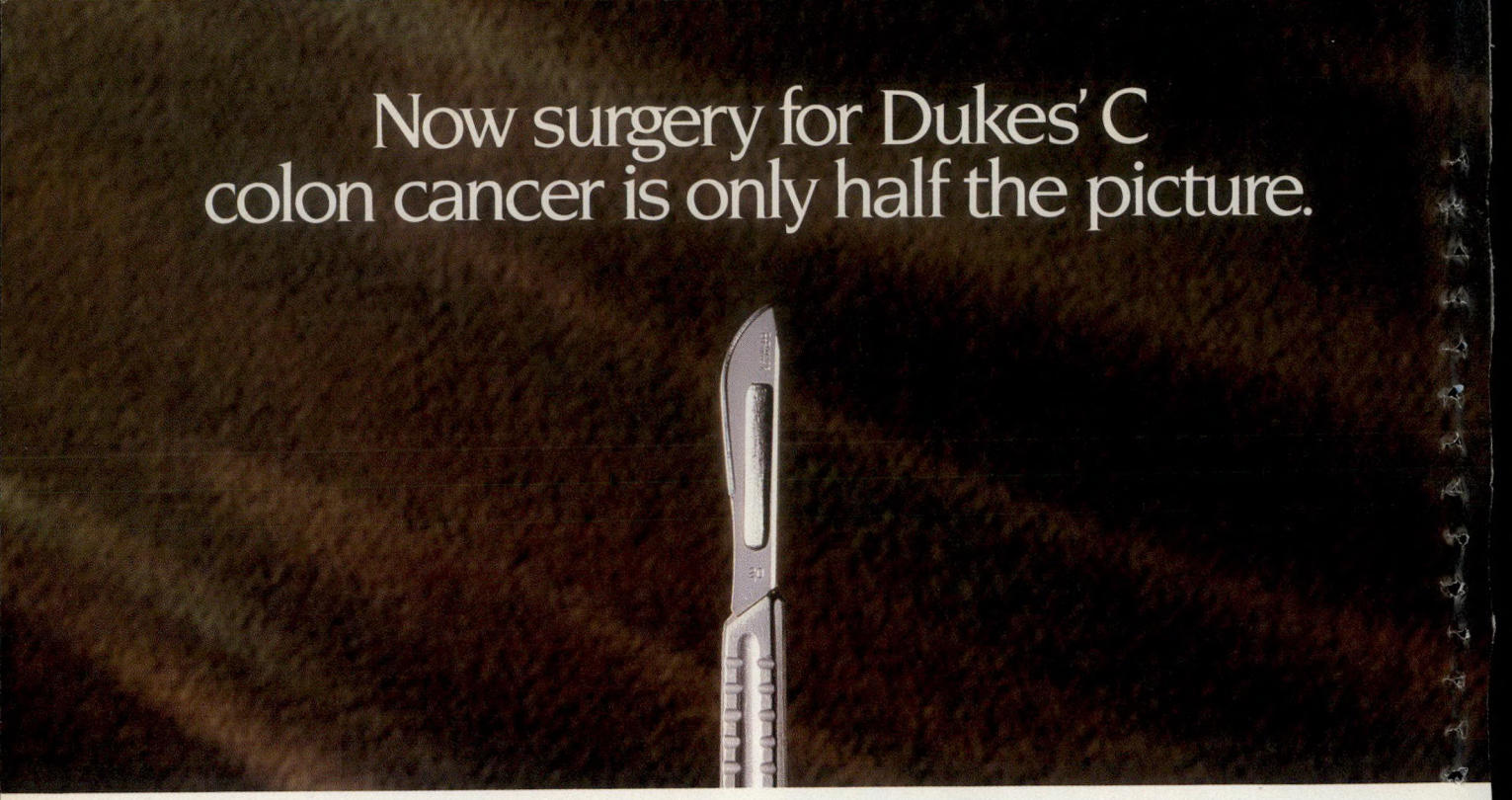

Ergamisol* + 5-FU. The first adjuvant therapy proven to reduce recurrence by 41%.

LEVAMISOLE AND FLUOROURACIL FOR ADJUVANT THERAPY OF RESECTED COLON CARCINOMA

Abstract Twelve hundred ninety-six patients with resected colon cancer that either was locally invasive (Stage B_2) or had regional nodal involvement (Stage C) were randomly assigned to observation or to treatment for one year with levamisole combined with fluorouracil. Patients with Stage C disease could also be randomly assigned to treatment with levamisole alone. The median follow-up time at this writing is 3 years (range, 2 to 5½).

Among the patients with Stage C disease, therapy with levamisole plus fluorouracil reduced the risk of cancer recurrence by 41 percent ($P < 0.0001$). The overall death rate was reduced by 33 percent ($P \approx 0.006$). Treatment with levamisole alone had no detectable effect. The results in the patients with Stage B_2 disease were equivocal and too preliminary to allow firm conclusions. Toxic effects of levamisole alone were infrequent, usually consisting of mild nausea with occasional dermatitis or leukopenia, and those of levamisole plus fluorouracil were essentially the same as those of fluorouracil alone—i.e., nausea, vomiting, stomatitis, diarrhea, dermatitis, and leukopenia. These reactions were usually not severe and did not greatly impede patients' compliance with their regimen.

We conclude that adjuvant therapy with levamisole and fluorouracil should be standard treatment for Stage C colon carcinoma. Since most patients in our study were treated by community oncologists, this approach should be readily adaptable to conventional medical practice. (N Engl J Med 1990; 322:352-8.)[1]

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New Bronchoscopic Instruments: a Toothpick and a Corkscrew

C.L.N. Robinson, MD, FRCS, FRCSC

Unusual foreign bodies require ingenuity to remove. I describe here two cases in which unusual instruments were used to remove unusual foreign bodies from the right and left lower-lobe bronchi of a 55-year-old man and a 6-year-old boy.

Case Reports

Case 1

During the fitting of a gold crown to a defective molar a 55-year-old dentist accidentally inhaled the crown when it slipped his colleague's fingers. The crown settled in the right lower-lobe bronchus (Fig. 1). Although the dentist did not experience any serious symptoms he did have minor wheezing on the right side of the chest. When I first saw the patient in the Emergency Department I thought the crown could be removed easily by bronchoscopy. However, when I tried to grasp the crown, which was lying with the blunt side down and was quite firmly impacted, with an angled alligator forceps, the leading edge was too slippery, and attempts to remove it simply pushed it further down the bronchus.

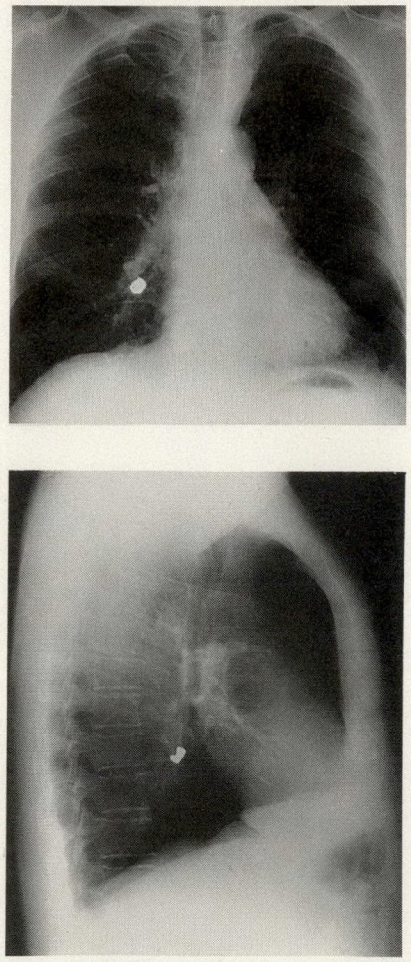

FIG. 1. Posteroanterior and lateral views showing metal (gold) crown in right lower-lobe bronchus.

To overcome this I had a "toothpick" instrument made (Fig. 2). It was 50 cm long, had a thickened, serrated handle and a small, sharp, angled point.

Two days later I made another attempt to remove the crown. With an assistant holding the broncho-

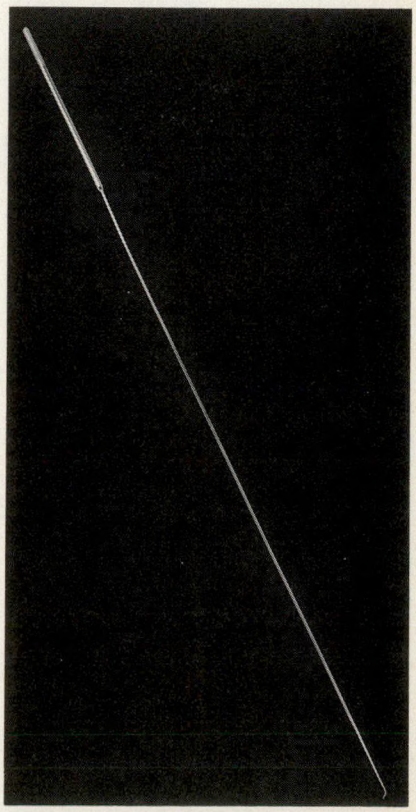

FIG. 2. "Toothpick" with 50-cm long handle and fine angled tip.

Emeritus clinical professor of surgery, Faculty of Medicine, University of British Columbia, Vancouver

Accepted for publication Nov. 27, 1989

Reprint requests to: Dr. C.L.N. Robinson, 604–750 West Broadway, Vancouver, BC V5Z 1H5

← For prescribing information see page 36

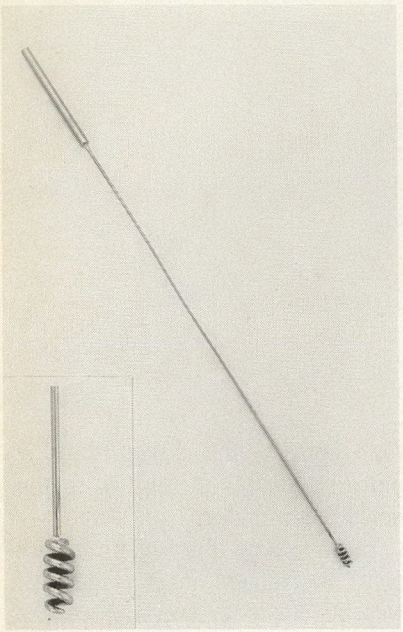

FIG. 3. Long instrument with corkscrew at end.

scope steady I was able to get the toothpick around the edge of the crown, rotate it enough to grasp the sharp edge firmly with an alligator forceps and remove it trailing. The crown was fitted correctly a few days later.

Case 2

A 6-year-old boy accidentally inhaled a plastic, cone-shaped head of a toy bullet, which became lodged in the left lower-lobe bronchus. It was pointed down and firmly impacted. The cylinder-like end of the bullet was pointed upwards making it impossible for me to grasp the bullet without damaging the wall of the bronchus. The cone end of the bullet had a tiny hole. Therefore I had a long instrument made with a corkscrew at one end (Fig. 3). The corkscrew was inserted through the hole, and the bullet was removed safely, trailing, without damaging the bronchial wall.

I wish to thank Keir & Sons, Vancouver for making the two instruments.■

SESAP VI Question

Item 145

Administration of polyvalent pneumococcal vaccine to a child who has undergone splenectomy

(A) virtually eliminates the risk of overwhelming postsplenectomy infection (OPSI)

(B) reduces the risk of OPSI by approximately one third

(C) is of no benefit unless given prior to splenectomy

(D) is of no benefit because many of the bacteria causing OPSI are not pneumococci

(E) is contraindicated for children who have undergone splenectomy for hematologic diseases. For the incomplete statement above select the best of the five completions.

For the critique of Item 145 see page 69.

(Reproduced by permission from *SESAP VI Syllabus; Surgical Education and Self-Assessment Program No. 6.* For enrolment in the Surgical Education and Self-Assessment No. 6, please apply to the American College of Surgeons, 55 East Erie St., Chicago, IL 60611.)

Detection of Micrometastases From Primary Breast Cancer

D.J. Courtemanche, MD;* A.J. Worth, MD, FRCPC;† R.W. Coupland, MD, FRCPC;‡ J.K. MacFarlane, MD, MSc, FRCSC§

The monoclonal antibody LICR-LON-M8 was used in a series of experiments to determine how an immunohistochemical technique could be used as a diagnostic test for micrometastatic disease in patients with operable, primary breast carcinoma.

Optimal tissue and antigen preservation was obtained with fixatives containing either picric acid or a heavy metal such as mercury to allow staining with the monoclonal antibody diluted to 1:12 000 to 1:16 000 from unpurified mouse ascites. Tissue affected by primary and metastatic disease stains in a characteristic fashion, which is distinct from benign breast tissue. All the ductal tumours stained positively for malignant cells with the monoclonal antibody preparation. Within the bone marrow, occasional granulocytes and granulocyte precursors stained positively if the endogenous peroxidase activity was incompletely blocked. These cells were readily differentiated from tumour cells on cytologic examination.

With these monoclonal antibody and immunohistochemical staining techniques it may now be possible to detect early micrometastatic disease in the bone marrow of patients with primary breast cancer.

L'anticorps monoclonal LICR-LON-M8 a été utilisé dans une série d'expériences visant à déterminer comment une méthode immunohistochimique pouvait être utilisée comme épreuve diagnostique des micrométastases chez les patientes souffrant d'un cancer primitif opérable du sein.

Une conservation optimale des tissus et de l'antigène fut obtenue à l'aide de fixatifs renfermant soit de l'acide picrique ou un métal lourd tel que le mercure et permettant une coloration avec l'anticorps monoclonal dilué à 1:12 000 ou 1:16 000 provenant d'ascite non purifié de souris. Les tissus atteints d'un cancer primitif ou envahis par des métastases se colorent de façon caractéristique, ce qui les différencient des tissus mammaires sains. Toutes les tumeurs canaliculaires ont donné une coloration positive en présence des préparations d'anticorps monoclonaux. Dans la moelle osseuse, quelques granulocytes et des précurseurs des granulocyctes ont pris la coloration quand l'activité de la peroxydase endogène était incomplètement bloquée. Ces cellules se différenciaient nettement des cellules tumorales à l'examen cytologique.

Avec ces anticorps monoclonaux et les techniques de coloration immunohistochimiques, il pourrait maintenant être possible de déceler précocément les micrométastases dans la moelle osseuse des patientes souffrant de cancer primitif du sein.

Breast carcinoma is the most common carcinoma in women, affecting approximately 6% of all women in their lifetime.[1] The biologic behaviour of breast cancer

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**Chief resident in plastic surgery, Department of Surgery, University of British Columbia, Vancouver*

†Clinical professor, Department of Pathology, University of British Columbia, Vancouver

‡Clinical assistant professor, Department of Pathology, University of British Columbia, Vancouver

§Professor and head, Division of General Surgery and head, Department of Surgery, St. Paul's Hospital, Vancouver

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Reprint requests to: Dr. D.J. Courtemanche, c/o Dr. J.K. MacFarlane, Department of Surgery, St. Paul's Hospital, 1081 Burrard St., Vancouver, BC V6Z 1Y6

appears to be inadequately predicted by standard staging methods. It remains unclear if this is a "systemic" disease at the time of diagnosis or if the tumour invades locally, nodally and then distantly over time. Some patients with locally advanced disease remain disease-free after treatment, and, in contrast, some patients with stage I lesions die early after treatment. For patients with stage I disease, the 5-year survival rate is 85% and for those with stage II disease it is 70%.[2] Clearly, a large number of patients are "under-staged" by currently available techniques.

Monoclonal antibodies provide sensitive probes for the investigation of biologic systems.[3-5] Many are reactive to breast carcinomas, but their clinical role has yet to be defined.[6-12] LICR-LON-M8 (M8) is one of several anti-breast monoclonal antibodies that have been made from membrane extracts of human breast milk.[6,7] The antigen is thought to be a T- or Tn-related precursor of the MN surface-antigen group.[13-15] This is an immune lipopolysaccharide, which appears to be very stable.

We describe several experiments using this antibody, performed in an attempt to develop a clinical test that would detect the presence of micrometastatic disease in the bone marrow of patients with primary breast carcinoma.

Methods

The monoclonal antibody M8 was supplied by Dr. B. Gusterson of the Ludwig Institute for Cancer Research in London, England, and by Dr. R. Buick of the Ontario Cancer Institute as unpurified ascitic fluid (with 0.1% NaN_3 as preservative). The technique of hybridoma production of monoclonal antibody has been described,[4] and the staining characteristics of M8 in benign and malignant breast tissues have been well documented.[6,7]

Fresh tissue (surgical specimens) and tissue previously fixed in 10% buffered formalin (BF) or picric acid formalin (PAF) were obtained from the pathology departments of the Vancouver General Hospital and the Cancer Control Agency of British Columbia. A variety of fixative solutions was used to preserve the fresh tissue.

Immunohistochemical staining was carried out by the avidin–biotin peroxidase complex method,[16] with M8 as the primary antibody.

Several experiments were conducted to determine the optimal method of fixing and staining the tissues.[17,18]

First, serial dilutions of the antibody were used to stain breast carcinoma tissue that was previously fixed in 10% BF or PAF to determine the optimal dilution of the antibody. Second, fresh tissue was fixed in each of 10% BF,[19] PAF,[20] B5 (sodium acetate–mercuric chloride–formalin fixative),[21] Bouin's solution[22] or 95% alcohol to determine the best method of preservation of the antigen. Following this, a variety of specimens of benign and malignant breast tumours were stained to verify the staining characteristics reported in the literature.[6,7]

From bone-marrow samples of patients without metastatic carcinoma, a series of spread and particle-section control slides were made. One aspiration specimen was crudely inoculated with dilutions of a cell suspension prepared from a fresh breast-carcinoma biopsy specimen. A series of crude dilutions of tumour cells in suspension were added to equal volumes of bone-marrow aspirate, and smears and particle sections were prepared and stained in a "spiking" experiment. Additionally, two biopsy specimens that yielded positive results on cytologic examination from patients with metastatic breast cancer were examined.

Slides were read independently by two pathologists, and all specimens had positive and negative controls.

Results

Initially, for the previously fixed and blocked tissue, the best results were obtained at a 1:16 000 dilution for tissue fixed in PAF and in a 1:4000 dilution for tissue fixed in 10% BF (Table I). The original specimen in BF was 2 years old, and, subsequently, for freshly fixed tissue a dilution of 1:12 000 was found optimal for all fixatives except 95% alcohol. The quality of the slides (freedom from artefact) was best for specimens fixed in Bouin's solution (Table II).

Using the above information, we examined breast biopsy specimens

Table I. Determination of LICR-LON-M8 (M8) Monoclonal Antibody Dilution for Optimal Staining

	Picric acid formalin ($n = 21$)			10% buffered formalin ($n = 14$)		
Dilution	**Stroma**	**Carcinoma**	**Benign**	**Stroma**	**Carcinoma**	**Benign**
1:2 000	++	+++	+	+	+++	−
1:4 000	++	+++	+	−	++	−
1:8 000	+	+++	−	−	+	−
1:16 000	−	++	−	−	−	−
1:32 000	−	+	−	−	−	−

− to +++ represents an arbitrary scale of staining intensity: − = no staining, + = weak staining, ++, +++ = progressively stronger staining.
n = total number of sections stained.

to confirm the staining characteristics of the antibody.[6,7] Benign breast tissue shows a characteristic apical luminal membrane staining, but tissue from carcinomas shows staining of the entire membrane as well as cytoplasmic staining that varies in intensity[23] (Fig. 1). All of the ductal carcinoma specimens tested stained with this antibody (Fig. 2). Specimens of primary breast carcinoma of other types did not stain as consistently[7] (Table III).

Normal bone marrow showed no staining other than stain absorbed by a few granulocytes and granulocyte precursors in endogenous peroxidase activity had not been completely blocked.[24,25]

Apart from the difficulty of placing a clump of tumour cells into a well-organized benign marrow, the inoculation of normal marrow with carcinoma cells worked relatively well. At 10^5 and 10^4 cells/mL, it was possible to differentiate clumps of cancer cells in the particle sections from the normal marrow (Fig. 3). These cells retained the cytologic characteristics of malignancy. At concentrations below 10^3 cells/mL no malignant cells could be detected (Table IV). No malignant cells were detected on any of the spreads. The incidental finding of two or three benign squamous cells contaminating one of the slides emphasized the ability of monoclonal antibody M8 to detect cells present at low concentrations.

Bone-marrow biopsy specimens containing large numbers of metastatic carcinoma cells were stained and showed the same characteristics as the primary tumours. The cells had the cytologic features of malignancy and could readily be differentiated from the normal bone-marrow cells.[26,27] Single cells within the section not readily seen on hematoxylin–eosin-stained sections could easily be visualized when the monoclonal antibody was used.[28,29]

Table II. Monoclonal Antibody Staining Quality Using Various Fixatives

Fixative	Monoclonal antibody dilution	Quality*
BF × 24 h × 3 h – 70% alcohol	1:1 500	Good
Bouin's solution × 24 h × 3 h – 70% alcohol	1:12 000	Excellent (better sections)
PAF × 24 h × 3 h – 70% alcohol	1:12 000	Excellent
B5 × 24 h × 3 h – 70% alcohol	1:12 000	Good (better sections)
90% alcohol × 24 h × 3 h – 70% alcohol	1:1 500	Good

* Histologic preservation and freedom from artefact.
BF = 10% buffered formalin, PAF = picric acid formalin, B5 = sodium acetate–mercuric chloride–formalin fixative.

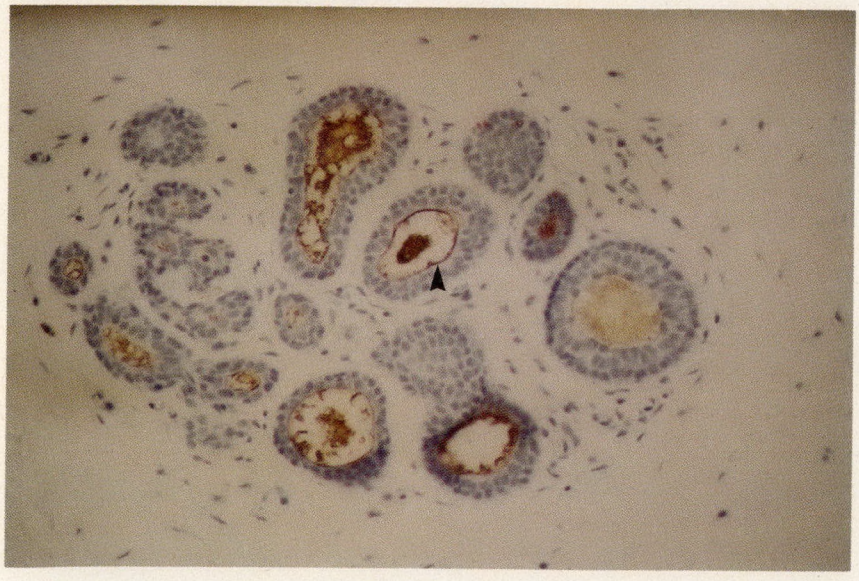

FIG. 1. Benign breast tissue showing apical luminal membrane staining with LICR-LON-M8 (M8) (arrow) (avidin–biotin peroxidase complex [ABC] technique with M8 as primary antibody and hematoxylin counterstain, original magnification × 250).

Discussion

The results show that it is possible to enhance the detection of micrometastatic disease in patients with primary breast carcinoma by using LICR-LON-M8 as a monoclonal antibody "probe." This has also been demonstrated with other monoclonal antibodies.[28–32] These results rest on the premise that normal bone-marrow cells will not stain, and that, in a patient with a primary breast carcinoma, any cells that stain within the bone marrow represent metastatic disease.[7]

Clinical verification of this assumption is lacking. Detection has been reported to correlate well with known risk factors for a poor prognosis.

Redding and colleagues[31] have shown that the bone marrow of patients with aggressive primary tumours, determined by standard grading techniques, was more likely to stain positive for carcinoma cells. Eighty-three percent of patients who had estrogen-receptor-negative

tumours with vascular and nodal invasion had bone marrow that stained positively for cancer cells compared with 11% of patients with estrogen-receptor-positive tumours without vascular or nodal invasion.

Dearnaley and associates[28] reported the short-term follow-up of a small group of patients whose bone marrow had been examined with the monoclonal antibody epithelial membrane antigen (EMA). The patients whose bone marrow tested positive had a shorter interval before clinical relapse occurred; however, their overall survival was not documented, perhaps because the follow-up was not long enough. Moreover, the characteristics of the primary tumour were not noted, therefore it is impossible to determine whether the positive bone marrow was an independent risk factor.

The experience gained in this set of experiments will be used in a prospective clinical trial. In this trial women who undergo surgery for primary breast carcinoma will, with informed consent, have four bone-marrow samples harvested at the time of their breast surgery. The tumours will be staged according to standard techniques and the bone-marrow samples will be evaluated separately in a double-blind fashion. The results of the bone-marrow screening will not be made available to the patients or their treating physician so as not to influence the patients' ongoing care.

Careful follow-up will be obtained and an assessment made of the prognostic implications of bone-marrow samples that test positive or negative as an isolated test in correlation with other methods of tumour evaluation.

Several questions remain to be answered:[33]

- Can positive bone-marrow staining be reliably detected in the clinical situation in patients with micrometastases?
- Does detection in this manner

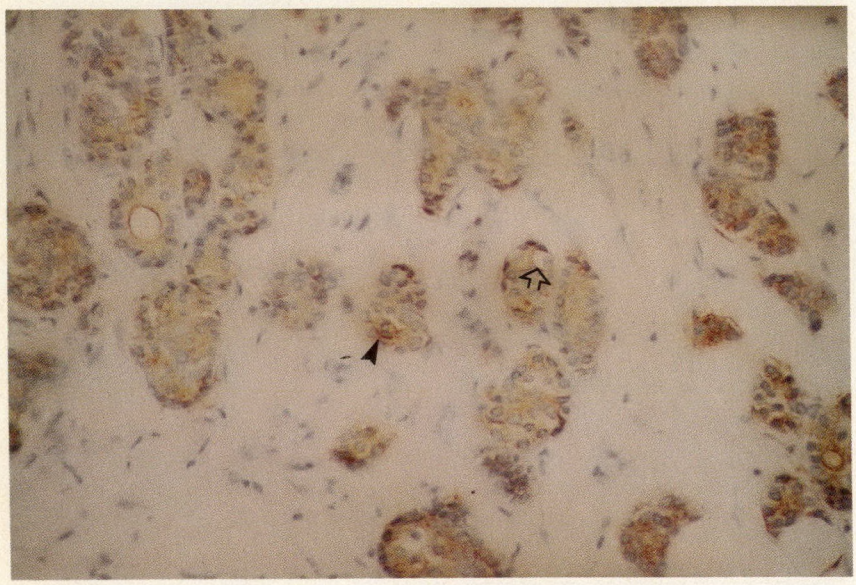

FIG. 2. Invasive ductal carcinoma showing holomembrane staining of varying intensity and cytoplasmic staining (compare cells indicated by arrow and arrowhead) (ABC technique with M8 as primary antibody and hematoxylin counterstain, original magnification × 250).

Table III. Pattern of Carcinoma Staining

Type of carcinoma	Grade	% staining (no.)
Infiltrating ductal	I	100 (6)
	II	100 (11)
	III	100 (8)
Medullary	All	75 (4)
Colloid	All	80 (5)
Lobular	All	100 (6)

Table IV. Detection of Cancer in Mock Positive Bone Marrow Specimens

Dilution, cells/mL	Cancer*	Comments
10^5	+	Cells clumped together
10^4	+	Cells clumped together
10^3	–	–
10^2	–	Squamous cells detected (see text)
10	–	–

*Possible cancer cells; + = positive, – = negative.

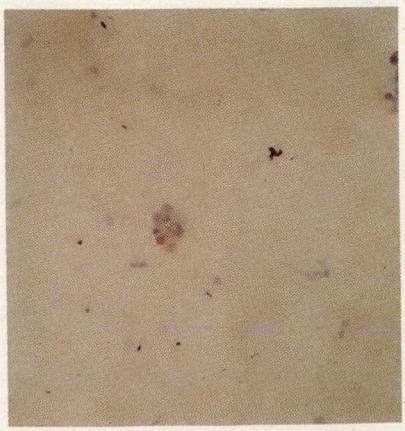

FIG. 3. Clump of malignant cells in benign marrow at dilution of 10^4 cells/mL (ABC technique with M8 as primary antibody and hematoxylin counterstain, original magnification × 250).

provide any new useful information about prognosis, compared with current methods of staging?

- Is the information likely to be of any benefit to the patient?
- Will patients with early metastatic disease be more likely to benefit from adjuvant chemotherapy?

Conclusions

Much remains to be learned about the biology of breast cancer. Monoclonal antibodies are just one of the tools being used in this learning process. At present there is no clearly defined role for the use of this powerful tool in the routine diagnosis and treatment of breast cancer.

Having shown that it is possible to detect breast cancer cells in an experimental situation, it is now necessary to test this hypothesis in the clinical setting. The monoclonal antibody M8 is only one of many such products being evaluated in the hope of improving our knowledge of the behaviour of carcinoma and our ability to treat patients.

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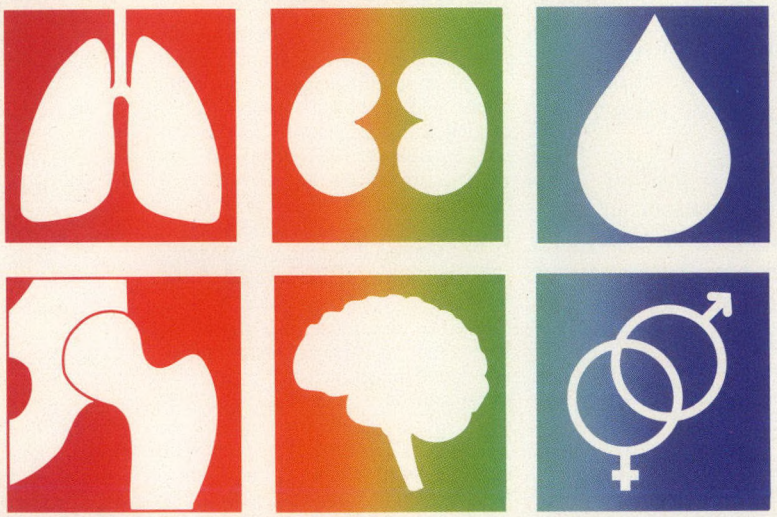

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Monoclonal Antibody LICR-LON-M8 Does Not Predict the Outcome of Operable Breast Cancer

D.J. Courtemanche, MD;* A.J. Worth, MD, FRCPC;† R.W. Coupland, MD, FRCPC;‡, J.L. Rowell;§ J.K. MacFarlane, MD, MSc, FRCSC¶

The prognostic value of the monoclonal antibody LICR-LON-M8, which has been shown to detect micrometastatic disease, was evaluated in a prospective, double-blind, clinical study of bone-marrow specimens from patients with operable breast cancer.

Four bone-marrow specimens, obtained from each of 50 patients at the time of excision of the primary breast tumour, were examined immunohistochemically, with LICR-LON-M8 as the primary antibody.

All of the primary tumour specimens demonstrated positive staining for malignant disease with LICR-LON-M8. The bone-marrow specimens of four patients demonstrated positive staining: three specimens were "suspicious" for malignant cells and one contained definite malignant cells on cytologic examination. This gave a 2% rate of detectable micrometastatic disease at the time the primary tumour was excised. Patient follow-up averaged 21.5 ± 9.1 months. The test results did not correlate with outcome. A negative test result with LICR-LON-M8 did not imply a better prognosis.

The authors conclude that examination of bone-marrow specimens stained with LICR-LON-M8 in patients with operable breast cancer is of no clinical value. Furthermore, the low rate of micrometastases detected is at variance with that reported by others. In view of the natural history of breast cancer, the authors believe that their results were not unexpected and they question the importance of other results.

La capacité pronostique de l'anticorps monoclonal LICR-LON-M8, lequel s'est montré capable de déceler les micrométastases, a été évaluée dans une étude clinique prospective, à double insu, d'échantillons de moelle osseuse provenant de patientes porteuses de tumeurs du sein opérables.

Quatre échantillons de moelle osseuse prélevés chez chacune de 50 patientes au moment de l'excision de la tumeur primitive du sein ont fait l'objet d'un examen immunohistochimique à l'aide du LICR-LON-M8.

Toutes les tumeurs primitives se sont révélées positives à la coloration au LICR-LON-M8. Les échantillons de moelle osseuse de quatre patientes ont présenté une coloration positive: trois échantillons étaient "douteux" pour la présence de cellules malignes et l'autre montrait définitivement des cellules malignes à l'examen cytologique. Ceci donne un taux de micrométastases décelables de 2% lors de l'excision de la tumeur primitive. La surveillance des patientes est en moyenne de 21.5 ± 9.1 mois. Les résultats des épreuves n'offrent pas de corrélation avec l'issue de la maladie. Un résultat négatif n'a pas signifié un meilleur pronostic.

Les auteurs concluent que l'examen des échantillons de moelle osseuse à l'aide du LICR-LON-M8 chez les patientes souffrant d'un cancer du sein opérable n'a pas d'intérêt clinique. De plus, le faible taux de micrométastases décelées diffère de ce qui est rapporté par d'autres. Vu l'histoire naturelle du cancer du sein, les auteurs croient que leurs résultats étaient prévisibles et ils mettent en doute l'importance d'autres résultats.

In the study of breast cancer, monoclonal antibodies are a research tool looking for a practical clinical application. Many laboratories have produced monoclonal antibodies that will react with human breast cancer cells.[1,2] Among these are the LICR–LON–M series of murine monoclonal immunoglobulin G antibodies produced originally at

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**Chief resident in plastic surgery, Department of Surgery, University of British Columbia, Vancouver*

†*Clinical professor, Department of Pathology, University of British Columbia, Vancouver*

‡*Clinical assistant professor, Department of Pathology, University of British Columbia, Vancouver*

§*Medical student (second year), University of British Columbia, Vancouver*

¶*Professor and head, Division of General Surgery and Department of Surgery, St. Paul's Hospital, Vancouver*

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Reprint requests to: Dr. D.J. Courtemanche, c/o Dr. J.K. MacFarlane, Department of Surgery, St. Paul's Hospital, 1081 Burrard St., Vancouver, BC V6Z 1Y6

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the Ludwig Institute for Cancer Research.[3,4] This series of monoclonal antibodies has been made to resemble membrane extracts of human breast milk.

A sample of one of these, LICR-LON-M8, was made available to the University of British Columbia for investigation. The hybridoma technique of monoclonal antibody production has been well described.[5] The material is supplied in the form of unpurified mouse ascites.

A preliminary series of experiments was reported in which the optimal methods of tissue fixation and staining were determined and the reported properties of this antibody verified.[3,4,6] The antibody reproducibly stained all ductal carcinoma specimens tested.

It was also determined that micrometastatic disease in the bone marrow could, theoretically, be detected, and the staining characteristics of carcinoma cells in marrow were noted. Other investigators have determined that as few as one malignant cell in 10 marrow cells may be detected in this way.[7]

We report a prospective study of the value of this monoclonal antibody as an independent staging technique in patients with operable breast cancer. The questions we were trying to answer were: Can we identify a subgroup of patients with operable breast cancer who have occult micrometastatic disease at the time the primary tumour is excised? and Does a positive test result give any independent prognostic information, and, if so, will this information benefit the patient?

To date several studies have demonstrated the ability to detect micrometastatic disease in patients with breast cancer; however, the value of this information remains unknown.[8] Positive test results correlate highly with already known risk factors for metastatic disease.[9]

Methods

Patients with primary, operable, breast cancer (stages I, II and IIIA) who were not involved in any other ongoing breast cancer study at the University of British Columbia were entered into the study. All appeared free of malignant disease on bone scanning and chest radiography and had normal results of liver function tests. No patient had a history of remote or current malignant disease of any other type.

Participation was voluntary. Consent forms were signed after an explanation of the study. The study protocol was approved by the University of British Columbia, Clinical Screening Committee for Research and Other Studies Involving Human Subjects and the medical ethics committees of the individual hospitals involved. Study data, which were collected on a standardized form, included the following: demographics, tumour history, clinical staging, pathological staging and relevant histologic detail, tumour hormone receptor status, immunohistochemical results for the primary tumour and the marrow specimens and clinical follow-up data.

The biopsies were done under general anesthesia just before excision of the primary tumour. Four bone-marrow biopsy specimens were obtained from each patient: two at right angles to each other from each posterior superior iliac spine. The biopsy specimens were fixed in Bouin's solution for 40 minutes and then in 70% alcohol.[10] They were dehydrated in alcohol, embedded in paraffin, sectioned and stained with hematoxylin and eosin and using the avidin–biotin peroxidase complex method (Vector Laboratories, Burlingame, Calif.) with the monoclonal antibody M8 as the

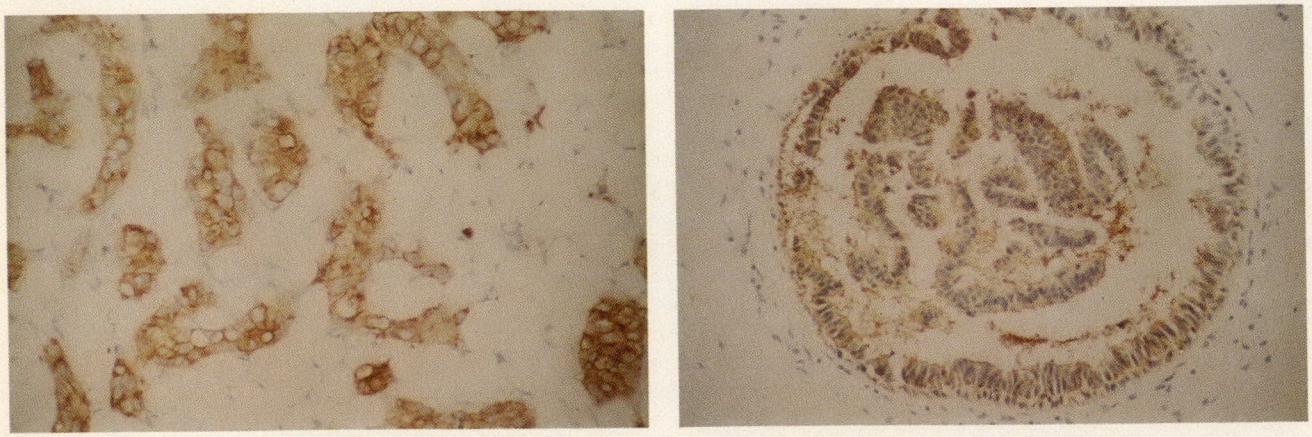

FIG. 1. Positive staining with LICR-LON-M8 antibody: (left) invasive ductal carcinoma; (right) intraductal carcinoma (avidin–biotin peroxidase complex technique with M8 as the primary antibody and hematoxylin counterstain, original magnification × 250).

primary antibody.[11] Positive and negative control studies were performed for each specimen.

Sections known to contain tumour cells from the formalin-fixed, paraffin-blocked, primary tumour specimen, were similarly stained with hematoxylin and eosin and were immunohistochemically studied as controls (Fig. 1).

Patients were followed up at 3-month intervals by the treating surgeon, family doctor or breast-tumour clinic of the Cancer Control Agency of British Columbia.

Ethics

The immunohistochemical test result was not released to the treating physicians, since the implications of the test result were not known at the start of the study, and it was important not to bias the ongoing care of these patients in any way.

Statistics

Data fitted to two × two tables for comparison of results between groups were analysed with Yates' modification of the χ^2 test. A p value less than 0.05 was considered statistically significant.

Results

Between March 1986 and September 1989, 53 patients were entered into the study. Complete data and up-to-date follow-up were available for 50 of these patients. One patient was lost to follow-up, one patient was excluded after diagnosis of a concurrent colonic carcinoma and one man was excluded.

Ages ranged from 28 to 93 years (mean 57.6 ± 12.8 years). Thirty patients were postmenopausal and 20 premenopausal.

The average follow-up was 21.5 ± 9.1 months. The 50 patients were divided into two groups: group 1 comprised 27 patients with follow-up of more than 2 years and group 2 contained 23 patients with follow-up of less than 2 years. This was done because the difference in recurrence rate between the two groups approached statistical significance (Table I).

In group 1, 10 patients had stage I disease, 12 had stage II and 5 had stage IIIA. In group 2, 12 patients had stage I disease, 10 had stage II and 1 had stage IIIA. There were 46 ductal and 4 lobular carcinomas. Forty-one tumours were estrogen-receptor positive (EP+); 6 showed vascular invasion (VI+) (Table II).

Thirty-two modified radical mastectomies were performed; 17 patients underwent segmental mastectomy with axillary dissection. In only two patients with stage I disease were the results of cytologic examination of the lymph nodes positive (Table III). All of the primary tumours stained with the monoclonal antibody, and four bone-marrow biopsy specimens did also.

Follow-up

Of the 22 patients having stage I disease, 10 were followed up for more than 1 year; 9 are alive and well, and 1 was free of disease when she died (Table IV). Of the 12 patients with stage I disease, followed up for less than 1 year, 11

Table I. Comparison of Recurrence Rate and Follow-up*

	Recurrence		
Follow-up yr	Yes	No	Total
< 2	2	21	23
≥ 2	7	20	27
Total	9	41	50

*$\chi^2 = 1.47$.

Table II. Stage and Type of Carcinoma in 50 Patients Studied

Group/stage	Type	ER+, no.	VI+, no.	VI−, no.
1/I ($n = 10$)	Ductal	9	8	1
	Lobular	1	1	–
1/II ($n = 12$)	Ductal	10	9	2
	Lobular	2	1	–
1/IIIA ($n = 5$*)	Ductal	5	4	2
2/I ($n = 12$)	Ductal	12	12	–
2/II ($n = 10$)	Ductal	9	5	–
2/IIIA ($n = 1$)	Ductal	1	–	1

*One of these patients had bilateral tumours.
ER+ = estrogen-receptor positive, VI+ = vascular invasion, VI− = no vascular invasion.

Table III. Treatment Received by the Patients in the Study

Stage	Number of patients	Treatment
I	11	Segmental mastectomy and axillary dissection with radiation to the remaining breast
	11	Modified radical mastectomy
II	8	Segmental mastectomy and radiation to the remaining breast
	14	Modified radical mastectomy
IIIA	1	Segmental mastectomy and radiation to the remaining breast
	4	Modified radical mastectomy
	1	Bilateral lumpectomy and radiation

are alive and well and 1, a 56-year-old postmenopausal woman, is alive with disease. She had local recurrence 11 months after segmental mastectomy and axillary dissection (0/8 lymph nodes tested positive for malignant cells on cytologic examination; tumour classification: T1N0M0, ER+, VI−). Three patients in group 1 with stage 1 tumours had bone-marrow specimens immunohistologically positive to M8; all are alive and well.

There were 22 stage II patients: 12 were followed up for more than 2 years and 8 were alive and well at the last follow-up, 1 who died was disease-free and 3 were alive with recurrent disease. These three were a 62-year-old postmenopausal woman who had recurrence 31 months after modified radical mastectomy (14/20 lymph nodes examined cytologically were positive for malignant cells; tumour classification: T2N1M0, ER+, VI+), a 94-year-old woman who had a recurrence 36 months after biopsy and radiotherapy (tumour classification: T2N0M0, ER+, VI−) and a 54-year-old woman who had lumbar metastases 22 months after modified radical mastectomy (3/12 lymph nodes were cytologically positive for malignant cells) and chemotherapy (tumour classification: T2N0M0, ER+, VI−).

The 10 patients who had stage II disease and were followed up for less than 2 years were all alive and well at the last follow-up. The bone-marrow specimens did not stain with M8 in any of the patients with stage II disease.

Of the six patients with stage IIIA disease, five were followed up for more than 2 years: one was alive and well, and one, a 64-year-old woman, was alive with disease. She had a recurrence 41 months after preoperative chemotherapy followed by modified radical mastectomy (0/12 lymph nodes cytologically positive for malignant disease) and postoperative chemotherapy (tumour classification: T3BN0M0, ER+, VI+).

Three stage IIIA patients died of their disease. One was a 58-year-old postmenopausal woman who had recurrence 18 months after modified radical mastectomy (0/18 lymph nodes cytologically positive for malignant cells; tumour classification: T3N0M0, ER+, VI−). The second was a 40-year-old premenopausal woman whose disease recurred 22 months after modified radical mastectomy (3/10 lymph nodes positive for malignant cells; tumour classification: T3N0M0, ER−, VI+). The third was a 40-year-old premenopausal woman whose disease recurred 17 months after modified radical mastectomy (8/9 lymph nodes cytologically positive for malignant cells; tumour classification: T3N2AM0, ER+, VI−).

The lone patient with stage IIIA disease and less than 2 years' follow-up, a 49-year-old premenopausal patient, is alive with disease. She had recurrent disease 12 months after bilateral lumpectomy, treated with radiotherapy and hormone therapy for bilateral tumours (tumour classification: T3BN0M0, ER−, VI+). Her bone-marrow specimens stained positively for malignant disease with M8.

Overall, the bone-marrow specimens of four patients stained positively with M8 (Table V). Three of these patients had stage I disease and were alive and well more than 2 years after treatment. The fourth had stage IIIA disease with bilateral aggressive disease (Fig. 2); she was alive with disease 12 months after initial treatment. The three patients with stage I disease had positive cells that were not cytologically typical of metastatic disease (Fig. 2).

The bone-marrow specimens of 46 patients stained negatively for malignant disease with M8. Three of these patients died of their malignant disease and five had recurrence. There was no statistically significant difference between groups 1 and 2 (Table VI).

Discussion

The aim of this study, which was

Table IV. Follow-up and Outcome by Stage and Group

Group	Stage	Number of patients	Outcome	Number
1	I	10	Alive and well	9
			Died without disease	1
	II	12	Alive and well	8
			Died without disease	1
			Alive with disease	3
	IIIA	5	Alive and well	1
			Alive with disease	1
			Died of disease	3
2	I	12	Alive and well	11
			Alive with disease	1
	II	10	Alive and well	10
	IIIA	1	Alive with disease	1

Table V. Patients Whose Bone-Marrow Biopsy Specimens Stained Positive Using LICR-LON-M8 Antibody

Group	Stage	Number of patients	Outcome	Cytologic findings
1	I	3	All alive and well	Possible malignant cells
2	IIIA	1	Alive with disease	Malignant cells

designed in 1985, was to evaluate an investigational tool as a practical clinical test. Although more complex and expensive methods of bone-marrow assessment, showing a theoretically higher yield of tumour cells, have been described, the techniques used in this study were selected because they could readily be applied to all patients.[12,13] This invasive test was designed to be acceptable to patients, surgeons and the members of the ethics committees.

At this level of sophistication the test has not proved to be of prognostic clinical value. More research needs to be done. At present we consider other methods too invasive or expensive to be used as routine clinical tests.

Large volumes of aspirated bone-marrow cells can be separated on a Ficoll–Hypaque gradient, and then the "buffy coat" can be selectively examined for tumour cells.[12] Porro and associates[13] reported that 17% of patients with breast carcinomas who had no cytologically positive lymph nodes, had cytologically positive bone marrow when this separation technique and immunofluorescent examination with the monoclonal antibody MBr1 were used. This remains a research rather than a clinical tool.

The low (2% to 8%) level of detection in our study is not surprising considering the nature of the disease and the patient population being studied.[14] Given the survival curves for breast carcinoma (5-year survival for stages I, II and IIIA: 85%, 70% and 50% respectively), only 13 of the 50 patients studied would be expected to relapse within 5 years. How many of these should we expect to have cytologically positive bone-marrow specimens at the time of surgical management of primary tumours? Indeed, Mansi and colleagues[15] found that only 2 of 82 relapse-free patients had cytologically positive marrow specimens 18 months after mastectomy. Other investigators, reporting higher detection rates, have not selected their patients prospectively and have more patients with advanced or prognostically unfavourable tumours.[16]

In this prospectively studied group of patients the rate of detection is so low that a prohibitive number of patients would need to be accrued to show a statistically significant difference at a twofold difference in outcome. In addition, although the presence of tumour

Table VI. Comparison of Recurrence of Disease and Immunohistochemistry*

	Recurrence of disease		
Immunohistochemistry	**Yes**	**No**	**Total**
Positive	1	3	4
Negative	8	38	46
Total	9	41	50

*$\chi^2 = 0.09$, not statistically significant.

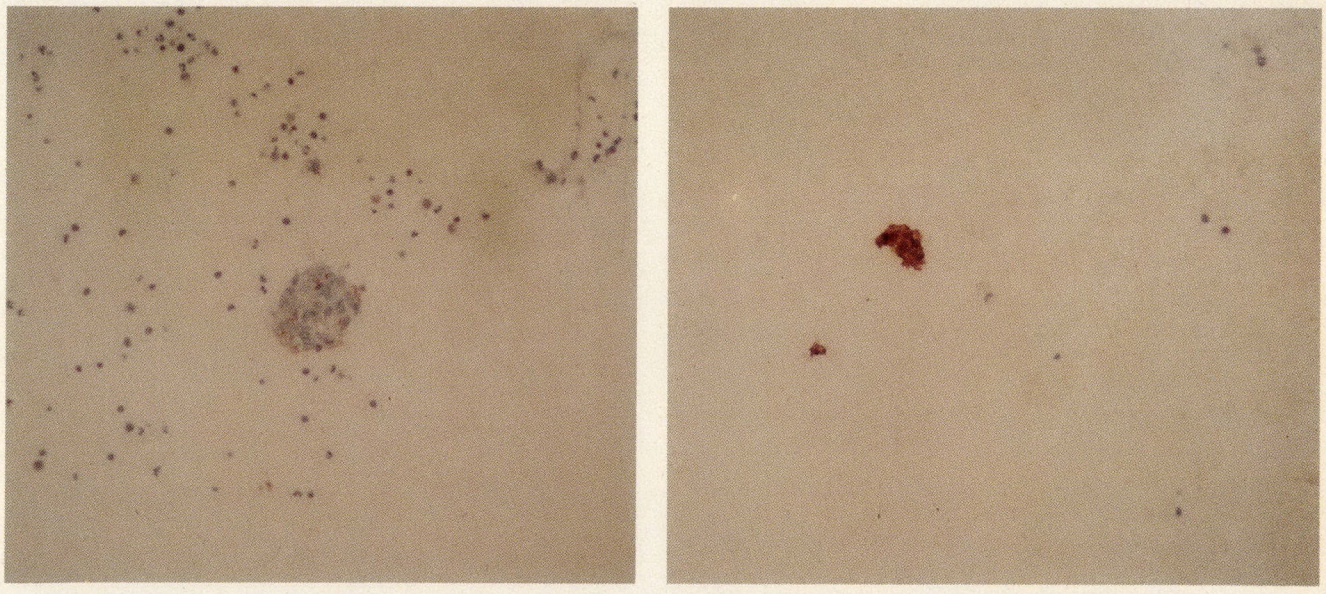

FIG. 2. Positive staining with LICR-LON-M8 antibody: (left) cytologically typical malignant cells in bone marrow; (right) not obviously malignant cells in bone marrow (avidin–biotin peroxidase complex technique with M8 as the primary antibody and hematoxylin counterstain, original magnification × 250).

cells in bone marrow can be detected, a positive result has not yet been shown to be an independent prognostic factor; the positive test results have only been correlated with tumour stage and grade. The cells detected may be cytologically typical for metastatic disease. They may theoretically also be degenerating nonviable clones of tumour cells or a reaction of myeloid cells to circulating tumour antigen excess. Other investigators have reported "suspicious" nonmyeloid cells not definitely metastatic carcinoma.[16]

Many cancer researchers are hoping that monoclonal antibodies will allow detection of the 15% of patients with stage I disease who suffer recurrence and die of their disease. Theoretically this would allow treatment of these patients with adjuvant chemotherapy and possibly improve their survival.[7]

Although monoclonal antibodies have enabled the detection of micrometastatic disease, more refinement is required to produce a useful clinical tool. Perhaps this type of investigation would be better applied to a subgroup of patients selected after standard tumour staging and grading.

Conclusions

In patients with operable breast cancer monoclonal antibodies can be used to detect occult micrometastatic disease. The rate of detectable micrometastatic disease is low (2%). There may be other reasons for positive staining of bone-marrow specimens. At present monoclonal antibody examination of specimens from four bone-marrow biopsy sites with LICR-LON-M8 antibody is not a practical prognostic test in patients with operable breast cancer.

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Nonoperative Management of Blunt Splenic Trauma in Adults

Wesley J. Stephen, Jr., MD;* Peter D. Roy, MD, FRCSC;† Philip M. Smith, MD;* Wesley J. Stephen, Sr., MD, FRCSC‡

The management of isolated blunt splenic trauma in adults is controversial. The authors present a series of 17 patients with blunt splenic trauma who were selected for nonoperative management. Only one patient eventually required surgery, for a ruptured spleen. Complications included pneumonia (two cases) and pleural effusion, atelectasis and ileus (one case each). There were no deaths. Five patients required transfusion, for a total of 17 units of blood. The mean length of hospital stay was 9.4 days. Comparison with a group of 17 patients treated operatively during the same period showed that those treated nonoperatively had fewer complications, required less blood and had a similar length of hospital stay. The authors conclude that nonoperative management of selected patients with isolated blunt splenic trauma is safe, if the patient's condition is closely monitored.

Le traitement des contusions et ruptures de la rate par traumatisme fermé chez l'adulte est un sujet de controverse. Les auteurs présentent une série de 17 cas initialement traités sans intervention chirurgicale. Une telle intervention ne fut éventuellement nécessaire que dans un seul cas de rupture. Parmi les complications, il y eut deux cas de pneumonie et un cas chacun d'épanchement pleural, d'atélectasie et d'ileus. Il n'y eut aucune mortalité. Seulement cinq malades eurent besoin de transfusion sanguine, pour un total de 17 unités de sang. La durée moyenne de séjour fut de 9.4 jours. Une étude comparative de 17 malades opérés pour traumatisme de la rate pendant la même période de temps révèle que les malades traités sans intervention eurent moins de complications, moins de transfusions et une durée de séjour comparable. Le traitement sélectif des traumatismes fermés de la rate par méthode nonopératoire peut être entrepris en toute securité lors qu'il y a surveillance clinique étroite.

Until recently, the standard treatment for all injuries to the spleen was splenectomy. Atelectasis, pleural effusion and early postoperative infection have long been recognized as complications of splenectomy. In 1952, King and Schumacker[1] described the syndrome of susceptibility to late infection after splenectomy in infants, and subsequent studies[2,3] outlined a small but clear risk of overwhelming gram-positive infection in patients of all ages after splenectomy. This led to the landmark studies from Toronto[4–6] on nonoperative management of splenic injury in children. However, the literature is lacking, and somewhat contradictory, with respect to the nonoperative management of isolated blunt splenic trauma in adults.

The concerns of nonoperative management include delayed splenic rupture, delay in recognizing other intra-abdominal injuries and a possible decrease in healing potential within the adult splenic architecture. Other potential disadvantages are increased requirement for blood products, longer hospitalization and the possibility of delayed operation for ongoing hemorrhage.

The purpose of this study was to review our experience with nonoperative management of isolated blunt splenic trauma in adults with respect to success rate, hospital stay and blood requirements. In addition, we looked at a group of patients who underwent early operation for isolated splenic trauma during the same period at the same institutions.

Patients and Methods

The charts of 66 patients who sustained blunt splenic trauma and were seen between January 1980 and December 1987 at Saint John Regional Hospital and Saint Joseph's Hospital, Saint John, NB, were reviewed. These two institutions are university hospitals that

From the Saint John Regional Hospital and Saint Joseph's Hospital, Saint John, NB, and the Department of Surgery, Dalhousie University, Halifax, NS

**Resident in surgery, Dalhousie University*

†Assistant professor of surgery, Dalhousie University

‡Lecturer in surgery, Dalhousie University

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Address reprint requests to: Dr. Peter D. Roy, Rm. 4125, Dickson Centre, Victoria General Hospital, Halifax, NS B3H 2Y9

are staffed with attending surgeons and general surgical residents. The diagnosis of blunt splenic trauma was made at laparotomy or from liver–spleen scanning, ultrasonography, computed tomography or from a combination of these investigations.

Of the 66 patients, 21 adults had other major multiple-system injuries and 11 were children under 14 years of age. These 32 patients were excluded, leaving 34 patients for study.

Patients were treated operatively or nonoperatively at the discretion of the attending surgeon and housestaff; there were 17 in each group. There were no formal guidelines for the choice of therapy. We could not reliably extract from the charts details on the presence or absence of clinical signs, except for evidence of hypotension on admission to the emergency department. There was no randomization of patients. Interestingly, all nine surgeons inolved in the study had patients in both the operative and nonoperative groups.

The patients treated nonoperatively were managed with bed rest, monitoring of vital signs, frequent examination by housestaff and surgeons and serial blood counts. Patients treated operatively underwent laparotomy promptly.

Findings

Demographically the two groups were similar in regard to age and mechanism of injury (Table I). Interestingly, all six women in the study were in the operative group. The reason for this is not clear.

Although it was difficult to ascertain physical signs and symptoms accurately, Table II compares two objective factors at the time of initial presentation: five (29%) of the operative patients presented with hypotension (systolic blood pressure less than 90 mm Hg) compared with only two (12%) of the nonoperative group; four (24%) of the nonoperative patients had delayed presentation (at 2, 7, 15 and 21 days after trauma), but only one (6%) of the operative group presented late (2 days after injury). This suggests that the patients in the operative group were more seriously injured.

The operative patients had different investigations from those in the nonoperative group (Table III). Thirteen (76%) of the operative patients had a positive diagnostic peritoneal lavage (DPL), whereas none of the conservatively treated patients had DPL. Three patients underwent immediate laparotomy on purely clinical grounds. In another operative patient the diagnosis was made by liver–spleen scanning. In the conservatively treated patients the diagnosis was most frequently made by liver–spleen scanning (14 patients), followed in frequency by ultrasonography (5 patients) and computed tomography (1 patient). Several patients had multiple investigations. Two patients with a negative ultrasonogram and one patient with a negative computed tomography scan subsequently underwent liver–spleen scanning, which gave positive results and, for the purpose of the study, was considered diagnostic.

There was no difference in the length of hospital stay (Table IV), but fewer patients treated nonoperatively required transfusions, and those who did so required less blood than patients in the operative group. Patients treated nonoperatively had fewer complications than those in the operative group (Table V).

Only one patient failed nonoperative management and required laparotomy with resultant splenectomy on hospital day 6. In the operative

Table I. Demographic Characteristics of Adults with Blunt Splenic Trauma According to Type of Management

Characteristic	Nonoperative ($n = 17$)	Operative
Mean age, yr	30.6	32.8
Sex, M/F	17/0	11/6
Mechanism of injury, no. of patients		
Motor vehicle accident	10	10
Sports	2	3
Fall	4	3
Assault	1	1

Table II. Features of Presentation

Feature	Nonoperative, number of patients (%)	Operative, number of patients (%)
Systolic blood pressure < 90 mm Hg	2 (12)	5 (29)
Delay in presentation	4 (24)	1 (6)

Table III. Comparison of Diagnostic Techniques

Technique	Nonoperative, number of investigations	Operative, number of investigations
Peritoneal lavage	0	13
Liver–spleen scanning	14	1
Abdominal ultrasonography	7*	0
Computed tomography	2*	0
Clinical diagnosis alone	0	3

*Includes two false-negative ultrasonograms and one false-negative computed tomography scan.

group, 15 patients underwent splenectomy; 2 had already achieved hemostasis and no further action was required. No patient underwent splenic repair or required reoperation. There were no deaths in either group.

Discussion

The epidemiologic characteristics of both groups of patients are consistent with those of previous reports with respect to age, sex and mechanism of injury. Although both of our groups appear to be representative of isolated blunt splenic injury, patients in our operative group were clearly more seriously injured. A clear selection bias is present, and any direct comparison between the two groups must be considered with this in mind. Nevertheless it is equally clear that transfusion requirements, complications and length of hospital stay in our nonoperative group were entirely within acceptable limits. Nallathambi and colleagues[7] warned clinicians about increased transfusion requirements and longer hospital stays for patients treated nonoperatively, but the findings of our study do not support this.

Only one patient in our nonoperative group required operation with splenectomy after a trial of nonoperative management, for a failure rate of 6%. This is in keeping with favourable reports,[8–14] citing failure rates of zero to 41%, in which failure is defined as the necessity for an operation, with or without resultant splenectomy. In sharp contrast, other reports[7,15–18] quote failure rates of 67% to 78%. The reason for this discrepancy is not clear. Possibly the unfavourable reports contained "unselected" patients, including those in shock, or the indications for eventual surgical intervention were more liberal.

It is interesting that no patient from the nonoperative group underwent DPL, but 13 patients (76%) in the operative group did, and all DPLs were positive. A positive tap was an indication for laparotomy in this study, which is is keeping with the Advanced Trauma Life Support guidelines[19] and current surgical practice.

In summary, it is safe to observe adult patients with isolated blunt splenic trauma as long as the patient's condition is stable at the time of presentation and close monitoring of clinical status is possible.

Table IV. Length of Hospitalization and Transfusion Needs*

Variable	Nonoperative	Operative
Length of hospital stay, d	9.4	9.6
Patients transfused, no.	5	12
Mean blood transfusion, units (range)	1.0 (0–5)	3.0 (0–9)

*Patients were not randomized. Selection bias may be present.

Table V. Complications*

Complication	Nonoperative	Operative
Pneumonia	2	2
Pleural effusion	1	2
Atelectasis	1	1
Ileus	1	3
Wound infection	0	1
Urinary tract infection	0	1
Late operation	1	0
Death	0	0
Splenectomy	1	15

*Patients were not randomized. Selection bias may be present.

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Wound Infections in Orthopedic Surgery: Effect of Extended Surveillance on Infection Rate

P. Pearce, RN; M. McKenzie, RN, BScN; G. Taylor, MD, FRCPC

Substantial evidence now exists that ongoing surveillance of surgical wound infections can contribute to reduced infection rates. What is not yet determined is whether surveillance should be limited to the postoperative hospital stay or should be continued after patient discharge. To determine the number of infections occurring after discharge, the authors contacted a random sample of their patients who did not have wound infections during their hospitalization after orthopedic surgery. This was done 30 days after the procedure. The authors selected 273 patients of 1375 who underwent orthopedic surgery over a 7-month period and were able to contact 199 (73%). At the 30-day follow-up 23 patients (11.6%) had wound infections, as judged by wound discharge and physician prescription of antibiotics in 20 and the patient's description of pus issuing from the wound in 3. During the same period postoperative wound infections were found in only 19 (1.5%) of 1278 patients who were subjected to in-hospital surveillance.

The authors conclude that, in patients who undergo orthopedic procedures, the majority of wound infections occur after discharge from the hospital and that infection rates based only on in-hospital surveillance greatly underrepresent true surgical wound infection rates for orthopedic procedures.

Il existe maintenant des preuves concluantes que la surveillance suivie des infections de plaies peut contribuer à faire diminuer le taux d'infections. Il n'a pas encore été déterminé si cette surveillance devait se limiter au seul séjour hospitalier ou si elle devait être poursuivie après le congé de l'hôpital. Dans le but d'établir le nombre d'infections qui surviennent après la sortie de l'hôpital, les auteurs ont communiqué, avec un échantillonnage aléatoire de leurs patients qui n'avaient pas souffert d'infection au cours de leur hospitalisation pour chirurgie orthopédique. Ceci eut lieu 30 jours après l'opération. Les auteurs ont choisi 273 patients parmi les 1375 qui avaient subi une chirurgie orthopédique au cours d'une période de 7 mois; ils ont réussi à en rejoindre 199 (73%). À en juger par la suppuration de plaie et la prescription d'antibiotiques chez 20 patients, et la description par le malade de pus s'écoulant de la plaie chez 3 autres, il y avait infection de plaie chez 23 patients (11.6%) au contrôle du 30e jour. Durant la même période, des infections postopératoires de plaies ont été observées chez seulement 19 (1.5%) des 1278 patients qui furent soumis à une surveillance dans un hôpital.

Les auteurs concluent que, chez les patients qui subissent une chirurgie orthopédique, la majorité des infections de plaies survient après le congé de l'hôpital, et qu'un taux d'infection basé uniquement sur une surveillance hospitalière sous-évalue considérablement les taux réels d'infections de plaies consécutives aux interventions orthopédiques.

From the Infection Control Unit, University of Alberta Hospitals, Edmonton

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Reprint requests to: Dr. G.D. Taylor, 2E3.11 Walter Mackenzie Centre, University of Alberta Hospitals, Edmonton, AB T6G 2B7

Evidence is accumulating that routine surveillance for surgical wound infections with feedback of data to practising surgeons can reduce overall wound infection rates. As a result there is increasing interest in this infection-control technique.[1-3] The Centers for Disease Control in Atlanta[4] and the Laboratory Centre for Disease Control in Ottawa[5] both recommend use of this technique, as did the Surgical Infection Society, which also endorsed it as a technique effective in reducing morbidity and costs related to surgical wound infection.[6]

For hospitals or surgical specialties embarking on this form of surveillance, consideration must be given to the need for long-term follow-up. A number of studies have compared post-discharge infection rates with those from inpatient surveillance alone.[5,7,8] However, the value of post-discharge surveillance may vary from one surgical subspecialty to another and from one institution to another. We have carried out surgical surveillance on wound infections after orthopedic surgery for over 2 years. We became concerned that our inpatient surveillance data might be unrealistically low, because of the early discharge or transfer of patients. Therefore we undertook a telephone survey of patients 1 month postoperatively to assess the value of this surveillance technique in our population.

Methods

The University of Alberta Hospitals (UAH) is a 1355-bed hospital,

← For prescribing information see page 81

acting as a tertiary referral centre for northern Alberta and western Northwest Territories. There are 11 practising surgeons in the Division of Orthopedic Surgery. Inpatient surgeon-specific wound surveillance began in March 1987.

On a daily basis, an infection-control practitioner (ICP) collects operating-room data sheets on all patients who undergo orthopedic surgery. Beginning 48 hours postoperatively, the ICP observes directly all surgical incisions not covered by plaster casts and returns every 48 to 72 hours for 2 weeks or until the patient is discharged. The ICP takes wound swabs when wound abnormalities are evident.

Wounds were classified on the clean–dirty spectrum by standard criteria.[9] Patients who died or were discharged less than 48 hours postoperatively were not considered in the analysis. Patients whose incisions were covered by plaster casts for the entire duration of hospitalization but in whom there was no suggestion of infection (e.g., fever, pain, swelling) were considered as noninfected and so entered into the denominator. A wound infection was diagnosed if: (a) the ICP observed pus issuing from the incision (excluding drain sites and stitch abscesses); (b) the ICP observed serosanguineous drainage and wound redness, and a culture was positive for a known pathogen (excluding common skin commensals); (c) deep-seated surgically related wound infection (e.g., osteomyelitis) was diagnosed by the surgeon, and the incision was not infected; or (d) the surgeon diagnosed wound infection associated with wound abnormalities that did not fit into any of the above categories.

The data were entered into a computer, and, with the use of the AICE software system designed for hospital infection control surveillance and data management,[10] monthly infection rates by surgical class were generated for each surgeon and the division as a whole. Surgeons were sent data on their own infection rates, with details on infections detected, as well as a report on the entire division's infection rates. Summaries of 6- and 12-month rates were also distributed.

Beginning in March 1988, for a 7-month period, patients who underwent regular inpatient wound surveillance but did not have a wound infection during that time were randomly selected by means of a random number generator in the AICE program, and contacted 30 days after their surgical procedure. An ICP telephoned the patients and asked a standardized set of questions. If the patient was still in the UAH the chart was reviewed. If the patient was in another hospital, the nursing station at that hospital was contacted. Patients who were not available on the first attempt were called on two further occasions, and if contact was still not made the patient was removed from the study. At this time a wound infection was diagnosed: (a) if a physician had examined the incision and had made a diagnosis of wound infection (as stated to the patient or implied by the prescription of treatment in association with wound abnormalities) or (b) if, having not seen a physician since discharge from hospital, the patient described pus issuing from the wound (excluding stitch abscesses).

This information was added to the basic information already entered into the computer.

Findings

During the 7-month survey period 1375 patients underwent orthopedic inpatient procedures: 1278 (93%) were suitable for inpatient wound infection surveillance; 336 (26%) had plaster casts covering their incisions up until discharge, so the incisions were not directly inspected but were assumed to be noninfected. Two hundred and seventy-three were selected for the 30-day follow-up. Of these, 199 (73%) were contacted. The 74 not contacted were similar by age and sex to the group contacted. Within the group of 199 patients contacted, 55 (28%) had not had the incision inspected because they had a plaster cast but had since had the cast removed or changed, so presence or absence of incisional abnormalities could be determined. When contacted 30 days postoperatively, only 20 were still in the UAH; 141 had been discharged home, 13 to a local community hospital and 25 to a rehabilitation hospital. Table I shows surgical wound infection rates for the inpatient survey period and the extended survey group. Of the 23 wound infections diagnosed in extended follow-up, 4 (17%) occurred in patients whose incision was not observed during their inpatient stay because of a plaster cast. Three infections (13%) were diag-

Table I. Wound Infections Found During Hospitalization and After Discharge in Patients Who Underwent Orthopedic Surgery

Type of procedure	In-hospital, no. infections/no. patients (% infection)	30 d after discharge, no. infections/no. patients (% infection)
Clean	11/1067 (1.03)	12/168 (7.1)
Clean–contaminated	0/49 (0)	1/4 (25)
Contaminated	0/18 (0)	0/2 (0)
Dirty	8/144 (5.56)	10/25 (40)
Totals	19/1278 (1.49)	23/199 (11.6)

nosed by the patient's description of pus and 20 (87%) by a physician's diagnosis (11 by the surgeon and 9 by the patient's general practitioner); 14 patients received antibiotic therapy.

Discussion

It is unlikely that any surveillance system could routinely detect all wound infections, nor is it necessary that all be detected, since the proposed mechanism by which wound infections are reduced by this technique is by permitting surgeon–surgeon comparisons, not comparison against an ideal. However, a surveillance system that detects very few of the actual infections runs the risk of being counterproductive by engendering a false sense of security among the recipients of the data. Other studies using active case-detection techniques similar to ours have shown that substantial numbers of infections can be detected by postdischarge surveillance;[6-8] none have shown such a large proportion as in our study. If the 199 randomly selected patients contacted 4 weeks after surgery were representative of the 1259 patients who did not have a wound infection at the end of the inpatient surveillance period, 145 wound infections would have been detected in this group. It is clear, therefore, not only that extended surveillance is much more effective at detecting wound infections but also that, by relying on inpatient surveillance, we have been greatly underestimating the true infection rate. If we add the 19 inpatient infections detected to the 145 infections that would be detected by 30-day telephone surveillance there would potentially be 164 wound infections in this population, only 12% of which were detected by our current surveillance technique.

The diagnosis of wound infection made by telephone survey may be questioned. Certainly, routinely bringing the patient back to the hospital for direct examination or even going to the patient's home to examine the incision[11] would be preferable. This is impractical for a long-term program, particularly when many patients do not reside in the city where the surgery was performed. We, like others, relied on a physician's diagnosis of wound infection[6-8] or, if the patient had not seen a doctor, on the patient's description of "pus" (discharge of opaque fluid from the incision). Extending the duration of follow-up during inpatient wound surveillance would not appear to be effective, since at the 30-day contact point very few patients were still in hospital. Consequently, some form of late follow-up appears necessary if a reasonable estimate of the true infection rate is to be made. Relying on patient- or doctor-initiated reporting of infection is most unlikely to detect consistent numbers of infections.[12,13] Some form of active surveillance is, therefore, necessary.

The clean wound infection rate of 7.1% found in this survey is much higher than that generally reported for inpatient surveillance programs[1,3] but is not dissimilar to rates found in other long-term follow-up studies.[6-8] The number of wound infections diagnosed is directly related to the method of detection, breadth of the definition and the duration of follow-up. Consequently, comparison of rates between studies should only be undertaken when these factors are available. The effects of extended surveillance on surgical infection rates are well documented in the medical literature.[6-8,14] In our patients, a far higher percentage of wound infection occurred after discharge (89%) than previous studies have documented. Those studies did not focus particularly on orthopedic patients, who may differ from other surgical patients in this regard. For example, the presence of a plaster cast prevents a proportion of inpatient wounds from being examined. This makes inpatient orthopedic wound surveillance difficult; 26% of the inpatients in our study could not have their incisions directly inspected during their hospital stay because of a cast. To delete such patients from the denominator would create a major gap in the completeness of our surveillance program, and, consequently, we chose to consider the wounds in these patients as not infected unless other signs of infection were present. Nevertheless, minor incisional abnormalities diagnostic of infection could be present and only become apparent after discharge when the cast is removed. This factor was a major contributor to the number of infections diagnosed after discharge.

Orthopedic patients may be discharged home or transferred to rehabilitation units outside the hospital more rapidly or frequently than patients who have undergone other types of surgery. Furthermore, because our hospital is a tertiary care hospital, many surgical patients are transferred to their local hospital for convalescence.

We have discussed our findings with our orthopedic colleagues. Although they support the wound surveillance program they wish to have data that reflect more closely the true infection rates, particularly for patients in whom the consequences of infection are most serious. We plan, therefore, to make extended surveillance a permanent part of our program for patients who undergo joint replacement and possibly to include other groups at a later date.

We thank the medical staff of the Division of Orthopedic Surgery, University of Alberta Hospital, for allowing us to observe their patients.

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Prescribing Information

ACTION

ERGAMISOL (levamisole hydrochloride) is capable of restoring impaired immune responses preferentially of the cell mediated type in compromised hosts. Therapeutic doses of levamisole restore to normal the functions of monocytes (phagocytes) and T lymphocytes but do not directly influence B cells.

Levamisole is rapidly absorbed from the gastrointestinal tract following a single oral ingestion of 150 mg. In patients with neoplastic disease, a mean peak blood level of 0.86 mcg/mL is attained within 2 hours of intake.

The half-life of elimination of levamisole alone is between 3-4 hours. The metabolites are eliminated more slowly with a terminal half-life of approximately 16 hours. Levamisole is extensively metabolized by the liver in man and excreted mainly by the kidneys (70% over 3 days). Approximately 5% is excreted in the feces. Less than 5% of the unchanged dose is excreted in the urine and less than 0.2% in the feces.

INDICATIONS

ERGAMISOL (levamisole hydrochloride) is indicated as adjuvant therapy in poor prognosis malignant melanoma following complete surgical excision and exclusion of metastatic disease. In such patients, levamisole has been shown to produce an improvement in relapse free survival and overall survival when compared to observation alone, particularly in patients aged 55 years or older.

ERGAMISOL is also indicated as adjuvant therapy, in combination with 5-fluorouracil, in patients with completely resected Dukes' stage C colon cancer. Evidence of metastatic disease must be excluded before initiating therapy. In patients with Dukes' stage C carcinoma of the colon, a regimen of levamisole plus 5-fluorouracil has been shown to produce significant reductions in both cancer recurrence and overall death rate.

CONTRAINDICATIONS

Levamisole is contraindicated in patients with a known hypersensitivity to the drug.

WARNINGS

ERGAMISOL (levamisole hydrochloride) has been associated with reversible leukopenia and agranulocytosis, therefore it is essential that appropriate hematological monitoring be done routinely during therapy with ERGAMISOL.

Patients should be instructed to report immediately any sudden change in their state of health which may be manifested by influenza-like symptoms (fever, lassitude, sore throat, shivering or sweating) so that appropriate hematological testing can be done.

Leukopenia (total WBC below 3000 mm^3) is not necessarily a sign of impending agranulocytosis; recovery is possible without withdrawal of the drug. However, with a reduced neutrophil count (less than 20% of the total white blood cell count) levamisole should be discontinued permanently. (Agranulocytosis is attributed to antibody formation and absorption of immune complexes. This process initiates complement activation and cell lysis; levamisole itself does not directly damage granulopoiesis.)

The HLA genotype B27 predisposes to the development of agranulocytosis, particularly in females with concomitant rheumatoid arthritis. The onset is frequently sudden and may be asymptomatic. Following discontinuation of levamisole, neutrophil counts normalize within a week to 10 days. There is no evidence that steroids or WBC transfusions are of significant therapeutic value; prophylaxis of infection during the acute phase of agranulocytosis should be an important consideration.

PRECAUTIONS

Drug Interactions: The therapeutic effect of levamisole may be antagonized by concomitant administration of corticosteroids.

Additional caution is necessary when levamisole is used in combination with other drugs potentially affecting hemopoiesis.

Levamisole has been reported to produce "ANTABUSE™"-like side effects when given concomitantly with alcohol.

ADVERSE REACTIONS

Approximately half of all patients treated with ERGAMISOL (levamisole hydrochloride) experience adverse effects of the medication. Due to the intermittent nature of the dosage schedule, drug discontinuation may not be necessary for successful resolution.

The adverse reactions observed when levamisole is used in combination with 5-fluorouracil are consistent with those anticipated if 5-fluorouracil is given alone in a comparable dose and schedule.

The incidence of adverse reactions for levamisole alone in malignant melanoma patients and for levamisole plus 5-fluorouracil in colonic cancer patients is presented in the following table:

	INCIDENCE (%)		
	LEVAMISOLE	LEVAMISOLE+5-FU	
		COLONIC	
ADVERSE REACTIONS	MELA-NOMA	INDUC-TION	MAINTE-NANCE
GASTROINTESTINAL			
nausea	24	37	56
vomiting	6	8	17
diarrhea		25	47
taste change	10	2	7
anorexia	1		
MUCOCUTANEOUS			
stomatitis	1	27	28
dermatitis	4	8	22
severe		1	1
alopecia		4	22
conjunctivitis		1	7
hyperpigmentation			2
HEMATOLOGICAL			
leukopenia	10		
2000 to 4000/mm^3		38	38
less than 2000/mm^3		7	2
thrombocytopenia			
50000 to 130000 /mm^3		4	18
less than 50000 /mm^3		2	4
agranulocytosis	1.4		
MUSCULOSKELETAL			
arthralgia/myalgia	8	2	4
NEUROLOGIC			
visual change			2
smell change		1	2
headache		1	5
dizziness/vertigo		1	4
ataxia			3
anxiety/irritability		2	2
depression		1	2
insomnia			1
somnolence			1
impaired thinking		1	2
OTHER			
fatigue/weakness		5	11
fever	8		
impaired liver function		1	2

SYMPTOMS AND TREATMENT OF OVERDOSAGE

There is no experience of overdosage with ERGAMISOL (levamisole hydrochloride). At high doses ERGAMISOL exhibits positive inotropic and chronotropic properties on heart muscle as well as convulsant properties. General supportive measures are recommended.

DOSAGE AND ADMINISTRATION

In patients with malignant melanoma

ERGAMISOL (levamisole hydrochloride) should be administered at a dose of 2.5 mg/kg given as a single daily dose, preferably at night, on 2 consecutive days every week. Higher doses are not recommended as they are associated with increased toxicity and have not been shown to provide any additional therapeutic benefit.

In patients with Dukes' stage C carcinoma of the colon

Levamisole plus 5-fluorouracil should be administered only by or under the supervision of qualified physicians, experienced in cancer chemotherapy, and well versed in the use of potent antimetabolites.

Therapy with ERGAMISOL may be initiated as soon after resection as patients are able to tolerate oral medication, but no sooner than one week and no later than five weeks after surgery.

ERGAMISOL should be administered orally at a dose of 50 mg t.i.d., for three consecutive days, every two weeks. This therapy should be continued for at least one year.

Administration of 5-fluorouracil should be timed to begin concomitantly with the second three day course of levamisole. The initial dosage of 5-fluorouracil should be 450 mg/m^2/day, given intravenously, for five consecutive days.

Four weeks following the initial five day course of 5-fluorouracil, patients should begin maintenance therapy on a once weekly basis with an intravenous injection of 5-fluorouracil at a dose of 450 mg/m^2. Treatment should continue for as long as levamisole is administered.

If the patient experiences stomatitis, diarrhea or leukopenia, the weekly 5-fluorouracil administrations should be deferred until these side effects have subsided. If these side effects are moderate to severe in intensity, 5-fluorouracil should be resumed with a 20% reduction in the dose.

Dosage Forms:

Availability: ERGAMISOL tablets 50 mg are available in blister packages of 36 tablets.

Storage: ERGAMISOL tablets 50 mg should be stored at room temperature and protected from moisture and light.

Product monograph available on request.

1. Moertel CG et al. Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. *New Engl J Med.* 1990;322:352–8.

NEW

℗ ERGAMISOL*

LEVAMISOLE HCl TABLETS

in combination with 5-fluorouracil

Detecting Breast Cancer After Reduction Mammoplasty

P.A. Clugston, MD; Q.R. Son-Hing, MB, ChB, FRCSC; J.K. MacFarlane, MD, FRCSC

Reductive breast surgery may give rise to parenchymal scarring that makes subsequent clinical and radiologic assessment of tumours difficult. The features that help distinguish benign from malignant lesions are discussed. Biopsy is still necessary. A screening protocol that includes preoperative mammography in patients at increased risk is proposed.

La chirurgie conservatrice du sein peut provoquer une cicatrisation parenchymateuse qui rend difficile l'évaluation clinique et radiologique future des tumeurs. Les caractéristiques qui aident à distinguer les lésions malignes des lésions bénignes sont exposés mais la biopsie demeure toujours nécessaire. Un protocole d'examen qui comprend la mammographie préopératoire chez les patientes à risque éléve est proposé.

Hypertrophy of the female breast is common and is often severe enough to cause negative effects both physically and psychologically. These effects can be alleviated by surgical reduction. However, the parenchymal scarring that may arise after surgery can interfere with clinical and radiologic examination of the breast for cancer. The incidence of breast cancer is such that it will develop in 1 in 11 women during their lifetime.[1,2] It is therefore important that we be able to identify lesions that may be malignant. We present two cases of breast cancer after reduction mammoplasty.

Case Reports

Case 1

A 53-year-old woman presented with an 8-month history of sagging and inversion of the right nipple. Fourteen years earlier she had had a bilateral mastopexy. No recent mammogram was available. There were no strong risk factors for breast carcinoma. She had undergone a hysterectomy and unilateral oophorectomy for menorrhagia at 44 years of age.

Physical examination revealed a mobile thickening, 2 to 3 cm in diameter, in the upper, inner quadrant of the right breast. The nipple was inverted and directed inferiorly (Fig. 1). There were no clinical findings to suggest metastatic disease. Mammography was arranged and she was referred to a general surgeon.

The mammogram revealed a spiculated mass lesion suggestive of carcinoma (Fig. 2). Fine-needle aspiration was carried out, and the aspirate was positive for malignant cells.

The patient underwent a modified right radical mastectomy. Pathological examination revealed a poorly differentiated, infiltrating, lobular carcinoma (Fig. 3); three of eight lymph nodes were positive for malignant cells. No signs of metastasis were found and she was referred for adjuvant chemotherapy.

Case 2

A 58-year-old woman had a remote (1973) history of stage II infiltrating ductal carcinoma of the right breast that had been treated by modified radical mastectomy followed by adjuvant radiotherapy to the chest wall and regional nodes. She had had postmastectomy reconstruction with a myocutaneous flap. A reduction mammoplasty of the left breast was performed in 1984 because of asymmetry. She had a revision of her mammoplasty in 1985. It is of note that she had been taking Climacteron (testosterone and estradiol in oil) from 1979

From the Department of Surgery, St. Paul's Hospital, University of British Columbia, Vancouver

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Reprint requests to: Dr. Q.R. Son-Hing, Ste. 808, 1200 Burrard St., Vancouver, BC V6Z 2C7

until 1987. She had also undergone a hysterectomy in 1968 for uterine fibroids.

Shortly after the revision mammoplasty she had noted firmness in the upper portion of her left breast. In late 1987 a firm ridge developed in the upper outer quadrant of the left breast, associated with nipple inversion and puckering of the overlying skin. When she was seen 4 months later, mammography revealed a poorly defined, spiculated lesion 3.7 cm in diameter. Open biopsy was performed, and pathological examination confirmed a moderately to poorly differentiated ductal carcinoma with dermal invasion.

The risk factors included a strong family history: both a first- and a second-degree relative had died of metastatic breast carcinoma postmenopausally. Initial mammography done in 1973 was interpreted as being consistent with bilateral fibrocystic disease. She had undergone mammography annually since her initial mastectomy until 18 months prior to this presentation.

Further examination was suggestive of metastatic disease in the liver, but the results were inconclusive and she was placed on a treatment protocol for locally advanced carcinoma.

Discussion

The Relation Between Breast Surgery and Cancer

The effect of surgical reduction of the female breast on the subsequent incidence of breast carcinoma is not known. Some believe that it may increase the risk of cancer. In 1957, at a meeting of the American Society of Plastic and Reconstructive Surgery, Maliniac reported a case of breast cancer after reduction mammoplasty, involving a free nipple graft, and proposed that damage to the mammary ducts gives rise to ductal stasis and may increase the neoplastic potential.[3]

It has also been hypothesized that removal of breast tissue proportionately decreases the number of foci for potential neoplasia and should therefore decrease the subsequent risk of carcinoma.[4] This view is supported by Snyderman and Lizardo,[5] who studied the number of malignant lesions found before or during surgery or in routine sectioning of the resected tissues after reduction mammoplasty. They found a frequency of 0.4%. This represents a three- to fourfold increase over the rate found in the general population and suggests that early occult lesions are being resected.[6] A recent study by Lund, Ewertz and Schou[4] supports this concept. They found a decreased relative risk of 0.59 for breast cancer after reduction mammoplasty, though this was statistically significant only after 10 years of follow-up. The relative risk was further decreased in women with reduction specimens weighing more than 600 g bilaterally. They concluded that women who undergo reduction mammoplasty for breast hypertrophy run no greater risk of breast carcinoma than does the general population and that after 10 years

FIG. 1. Case 1. Inverted, inferiorly directed nipple in breast with carcinoma.

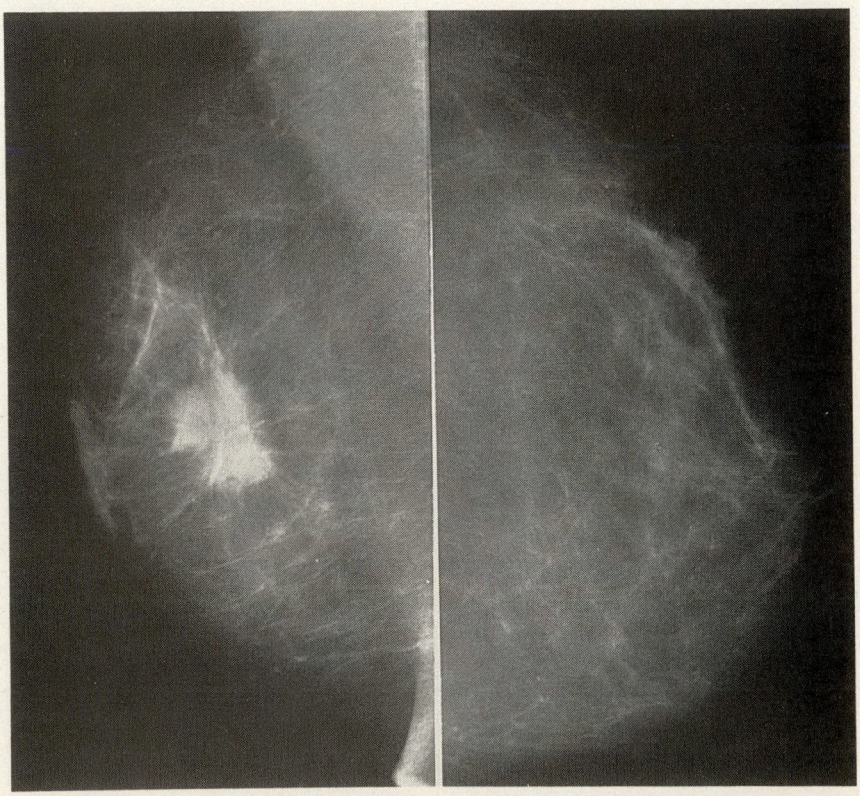

FIG. 2. Case 1. Mammogram showing 4-cm spiculated mass lesion with associated thickening and retraction of overlying skin.

they show a significantly decreased risk.

Differentiating Benign Postoperative Changes From Carcinoma

Reduction mammoplasty could, perhaps, lead to the earlier detection of evolving tumours by allowing more accurate clinical and self-examination than is possible with large, pendulous breasts.[7] However, mammography performed after reduction mammoplasty may reveal changes similar to those associated with carcinoma.[2] Mammographic or clinically palpable masses seen postoperatively may represent scarring, deep-seated hematoma, fat necrosis, benign mammary disease or malignant disease; thus, assessment of these patients is difficult.[8] If mammography is to be of diagnostic value we must recognize the changes that may be seen in the breast, after either breast biopsy or reduction mammoplasty.

Postoperative benign mammographic changes can be divided into two major types: soft-tissue changes and calcifications. The soft-tissue changes include skin thickening and retraction, architectural distortions and asymmetric densities with spiculated or irregular margins and typically a central lucency.[2,9,10] Calcifications are coarser and less clustered in lesions that are benign. Iatrogenic lesions are most commonly present in the periareolar and inferior pole tissues, representing the areas of maximal surgical trauma and subsequent parenchymal scarring.[2]

Mammographic changes suggestive of malignant disease, on the other hand, include asymmetric densities, mass lesions with irregular or spiculated margins and central opacity, thickening and retraction of the overlying skin, and punctate, clustered microcalcifications.[10,11]

Other factors differentiating postoperative mammographic changes from those of malignant disease include the tendency of benign changes to resolve naturally and the lesser symmetry of spiculations, which also lack continuity with any overlying skin changes.[2,9] Although these features are helpful, they are often inadequate, and tissue biopsy is required to differentiate between malignant and postoperative benign iatrogenic lesions. Fine-wire localization techniques may be necessary for abnormalities that are not palpable.

Clinical findings may also be helpful, in that palpation of a benign scar typically reveals a vague thickening of a size that corresponds to the mammographic abnormality, whereas an infiltrating carcinoma typically is firmer and larger than the mammographic abnormality.[9]

Screening Guidelines

Guidelines for surveillance in women who seek or have had breast reduction surgery would help physicians identify, appropriately investigate and treat any malignant lesions that do develop. We offer a screening protocol for this purpose (Fig. 4), which includes monthly self-examination and regular examination of the breast and regional lymph nodes by a physician or experienced nurse clinician.

Preoperative and early postoperative mammography (at 3 to 6 months) would help delineate changes occurring secondary to surgery and rule out occult preoperative lesions. Along with clinical and self-examination of the breast, mammography must be considered in women more than 35 years old or with risk factors for breast carcinoma. Further mammography should be requested on the basis of results and according to the recommendations of the American Cancer Society (baseline mammography at 35 to 40 years of age, periodic examinations between the ages of 40 and 50 years and annually after the age of 50 years).[6]

Successive mammography in a given patient should be carried out

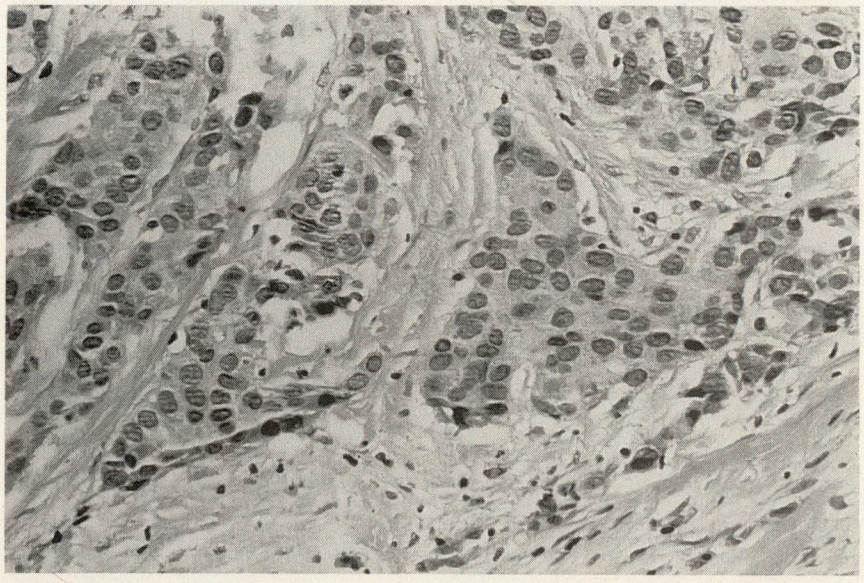

FIG. 3. Case 1. Section of breast tissue shows presence of poorly differentiated infiltrating lobular carcinoma (hematoxylin and eosin, original magnification × 1000).

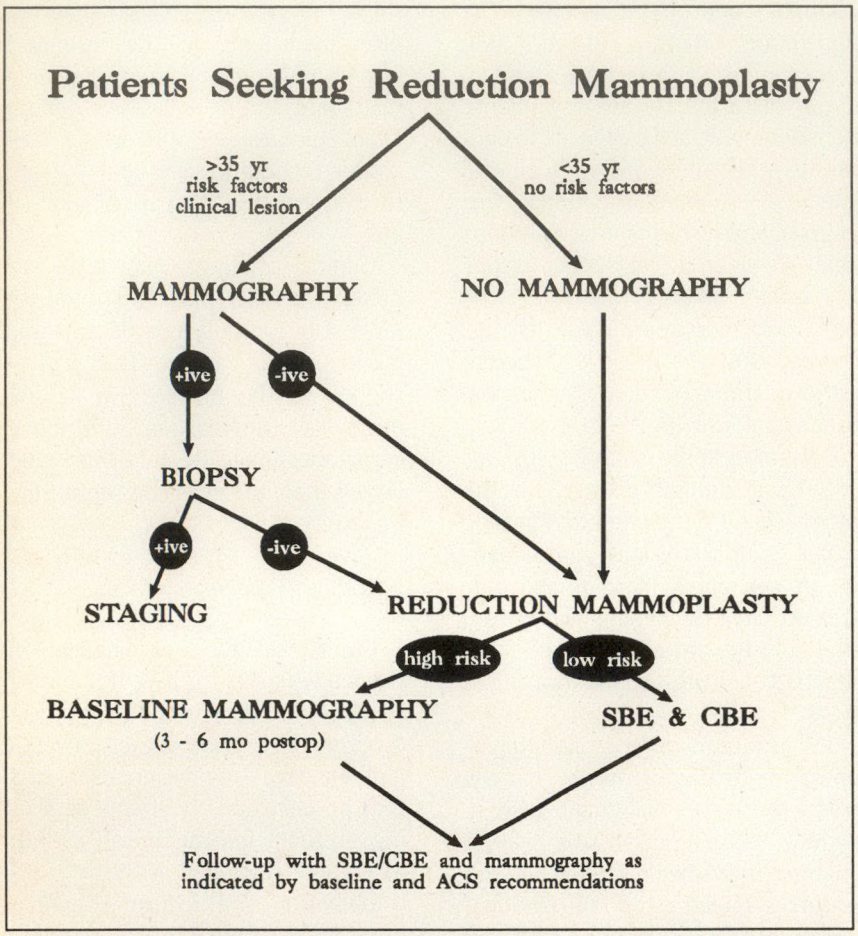

FIG. 4. Algorithm for screening in patients who undergo reduction mammoplasty. SBE = self breast examination, CBE = clinical breast examination, ACS = American Cancer Society.

at the same radiology suite to facilitate comparison of initial and follow-up films. The responsibility for appropriate mammographic evaluation should be that of both the primary care physician and the surgeon involved.

In those who, like our second patient, have had surgery for breast cancer and seek a reduction mammoplasty of the other breast to regain symmetry, a prophylactic mastectomy and immediate reconstruction might be considered. Either a silicone gel prosthesis or a pedicled regional flap could be used for reconstruction. This could negate the otherwise increased chance of a second primary developing and avoid the difficulties associated with mammographic and clinical assessment of the breast after reduction.

The use of a consistent screening protocol in women who either plan to have or have had reduction mammoplasty could lead to earlier detection of malignant disease, thereby reducing the overall morbidity and mortality.

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A Simplified Protocol for Banking Bone From Surgical Donors Requiring a 90-Day Quarantine and an HIV-1 Antibody Test

A.J.P. La Prairie BSc, TBS;* M. Gross MB, FRCS, FRCSC†

The banking of femoral heads from patients who undergo total hip arthroplasty provides a valuable resource for orthopedic surgery. Quality assurance of the banked bone used in clinical procedures requires documented policies for screening, procuring, storing and distributing.

Potential donors are screened at the time of donation for malignant disease, possible communicable disease, sepsis and high-risk life-styles. After negative culture results are confirmed and appropriate documentation has been completed, the bone is frozen at −70°C. A quarantine period of 90 days follows. The donor is followed up 90 days or more postoperatively. At that time written consent is obtained for donation of the recovered tissue to the bone bank and for serology testing for human immunodeficiency virus (HIV-1) antibody, hepatitis B surface antigen (HBsAG), hepatitis B core antibody (HBcAb) and syphilis, and the donor is rescreened for contraindications.

This protocol meets or exceeds all existing standards. The combination of obtaining consent and serology testing at 90 days streamlines the logistics of banking bone from surgical donors.

La conservation des têtes de fémurs provenant des patients qui subissent une arthroplastie complète de la hanche est la source d'un matériau d'une grande valeur en chirurgie orthopédique. L'assurance de la qualité des os conservés pour les interventions futures exige l'usage de politiques établies pour effectuer la sélection, le prélèvement, la conservation et la distribution.

Au moment d'effectuer leur don, les donneurs potentiels sont soumis à des épreuves de dépistage du cancer, des maladies transmissibles, des infections et des modes de vie à risque élevé. Après confirmation des résultats négatifs par culture et après obtention de la documentation appropriée, l'os est congelé à −70°C. Une période de quarantaine de 90 jours suit. Le donneur fait l'objet d'une surveillance postopératoire d'au moins 90 jours. À ce moment, le donneur signe une formule de consentement pour le don du tissu prélevé et pour des épreuves de dépistage sérologique des anticorps au virus immunodéficitaire humain (VIH-1), de l'antigène de surface du virus de l'hépatite B (HBsAG), des anticorps à l'antigène nucléocapsidique de l'hépatite B (anti-HBc) et pour le test VDRL; le donneur fait aussi l'objet d'un nouveau dépistage des contre-indications.

Ce protocole rencontre ou dépasse toutes les normes actuelles. L'obtention après 90 jours du consentement écrit, associée au épreuves de dépistage sérologique rationalise la logistique de la banque d'os provenant de donneurs chirurgicaux.

From Victoria General Hospital, Halifax

**Bone-bank technologist, Victoria General Hospital, Halifax. Certified tissue bank specialist with the American Association of Tissue Banks*

†Assistant professor of surgery, Department of Surgery, Division of Orthopedics. Medical director, Bone bank, Victoria General Hospital, Halifax

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Reprint requests to: Mr. A. La Prairie, Bone bank, Rm. 6–039, Victoria General Hospital, Halifax, NS B3H 2Y9

Femoral heads and other bones from patients treated surgically for such conditions as osteoarthritis and hip fractures are an available resource for orthopedic surgery. Common uses of allogeneic banked bone are as follows: (a) re-establishing structural bone stock;[1–3] (b) enhancing bone fusion (spinal surgery);[4–7] and (c) enhancing osseous integration of prostheses in arthroplastic surgery.[8–10]

Autogeneic bone is the graft of choice.[11,12] It has several advantages: there is no immune response or possibility of viable peripheral osteoblast cells and no chance of disease transfer. However, lack of sufficient available bone, increased surgical time, blood loss associated with harvesting of autogenous grafts, pain at the donor site and morbidity provide sufficient arguments for the use of allogeneic banked bone.[2–6,13–17]

Quality assurance of banked bone requires documented standards for donor selection, tissue recovery, preservation techniques, storage, record keeping and distribution.[18] These allograft femoral heads must be free of potentially transmissible diseases and sepsis. In 1988, the first documented case of human immunodeficiency virus (HIV) transmitted from a femoral head transplant was reported.[19] This motivated a proposal at a recent Canadian conference on allografts in orthopedic surgery that a test for the HIV antibody be done 90 days postoperatively on all living bone donors.[20] The American Association of Tissue Banks (AATB) issued a revision to

its standards.[21] As of January 1988, the association advised that: (a) an absolute quarantine be placed on all tissues from living donors for at least 90 days; (b) after 90 days the donor be tested for the HIV antibody; and (c) the tissue be released for distribution only if the results of the tests for the HIV-1 antibody are negative.

Protocols for banking bone from surgical donors have been well established[4,15,16,22-24] but do not include the required quarantine and testing of the donor at 90 days for HIV-1 serology.

In a recent survey of Canadian hospitals[25] it was concluded that many inadequacies exist in the operation of bone banks, including lack of consent from living donors and testing for the HIV-1 antibody.

In light of the increased interest in allograft bone transplantation, the possibility of transmitted disease and the medicolegal implications, we believe that a review of the practice of banking bone from surgical donors is due. This review must include reference to the new standards in HIV testing and address the required patient consent for both release of tissues and the confidential serologic testing.

A protocol has been established at the Victoria General Hospital in Halifax (Fig. 1) that meets or exceeds all documented standards of the AATB, the Centers for Disease Control in Atlanta and the US Food and Drug Administration. The protocol addresses the required written consent for donation and serologic testing and the 90-day quarantine followed by HIV antibody testing. We believe this protocol provides necessary guidelines for Canadian bone banks.

Methods

The osteoarthritic patient receiving a hip prosthesis is screened by the surgeon for contraindications (Table I). Biopsy specimens (2 × bone nibbles, not swabs) are taken from the femoral head for aerobic and anaerobic cultures. The bone is then soaked in a 10% Proviodine solution, placed in a plastic disposable jar (500 mL), sterile-wrapped sequentially with three freezer bags and passed off to the circulating nurse. An operating-room drape is added for protection, and a patient addressograph label is attached (including name, identification number and date of birth). The donor information form is filled out, including the surgeon's name, the donor's name, identification number, blood type, Rh factor, confirmation of screening, diagnosis and surgery performed. The form is signed by the surgeon and the circulating nurse. The wrapped femoral head is placed in a locked refrigerator maintained at 5°C and equipped with temperature monitor and alarm. The bone bank is notified. All documentation is sent to the bone-bank office.

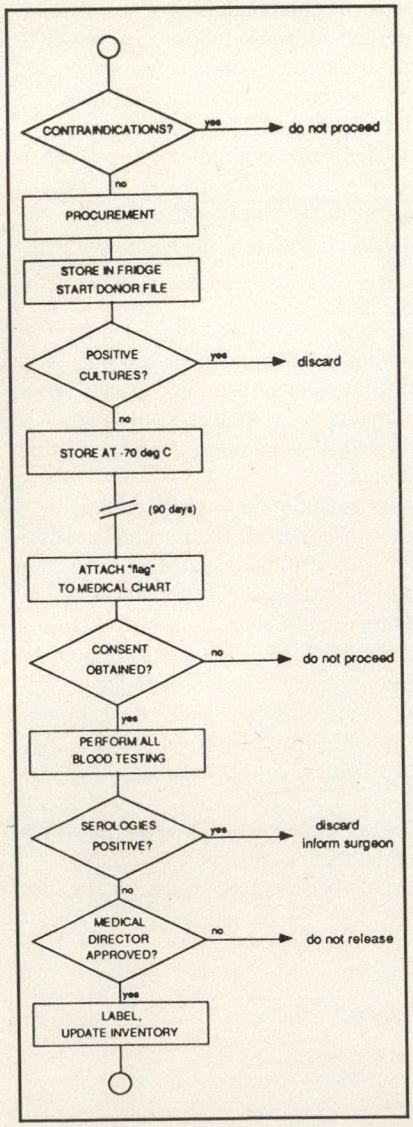

FIG. 1. Flow chart of process required to place acceptable donor femoral head in bone bank.

Initial aerobic and anaerobic culture results are reported (by phone) to the bone bank after 48 hours. If they are negative, the bone is transferred to a freezer maintained at −70°C and equipped with high- and low-temperature alarms. A technologist is on call at all times in case the unit fails. Access to this freezer is limited to the technologist and the bone-bank director. A chart recorder is in place to confirm maintenance of temperature. Once a week the freezer temperature monitors and alarm are checked (calibrated if necessary) and the findings documented.

A confidential donor file, complete with an assigned unique donor number (e.g., 89–101) is maintained at the bone bank. A final report of the results of the cultures

Table I. Contraindications to Donation of Bone to the Bone Bank

Recurrent or chronic infections
Systemic viral infections
History of viral hepatitis
Malignant disease
Slow nerve viruses (Creutzfeldt–Jakob disease, rabies) or history
Metabolic bone diseases (e.g., rheumatoid arthritis)
Long-term steroid therapy
Disease of unknown etiology (systemic lupus erythematosus, Alzheimer's disease, rheumatoid arthritis)
High-risk life-style or history
Recipients of human derived growth factor hormone

is sent to the bone bank after 6 days. A report of positive culture results is brought to the attention of the bone-bank director for interpretation.

A bone-bank follow-up sticker (Fig. 2) is sent to the medical records department at the end of the 90-day postoperative quarantine. This "flag" is placed on the outer cover of the outpatient chart to remind the surgeon to obtain consent and samples for serologic testing at the clinical follow-up, at least 90 days after the tissue was harvested.

At the clinic, the patient's social and medical history and postoperative recovery are reviewed against any further possible contraindications to donation. Written consent is obtained for donation of bone and for serologic testing to screen for the HIV-1 antibody, hepatitis B surface antigen (HBsAG), hepatitis B core antibody (HBcAb) and syphilis (VDRL test). Test results are directed in confidence to the bone-bank medical director.

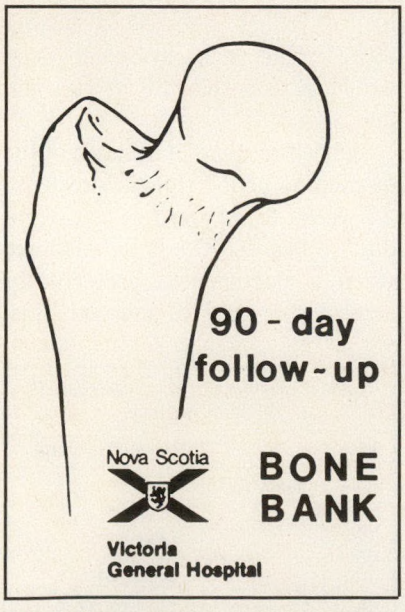

FIG. 2. Large sticker applied to patient chart after 90-day quarantine period. Sticker acts as "flag" to remind physician to obtain written consent and serologic testing.

If the patient refuses consent, the refusal is noted in the bone-bank file, and the bone is discarded. Abnormal results for any of the serologic tests mandates that the femoral head be subjected to further clinical study and that it be discarded if the test results are positive. All abnormal results are reported to the surgeon.

When the results of the serologic tests, the consent forms and the laboratory reports are complete, the donor file is reviewed and signed by the bone-bank medical director. The tissue is labelled with the unique donor number and is placed in the available bone inventory section of the bone-bank freezer, and the inventory list is updated.

The surgeon may request a femoral head from the bone bank. A minimum of 24 hours' notice is required to confirm the availability of Rh-compatible bone-graft material and to deliver it to the operating room on time. Every effort is made to use bone-graft material that has been donated by one of the surgeon's own patients.

The file for that femoral head is then rechecked by the technologist, its distribution is noted, and it is delivered to the operating room, complete with instructions and a recipient form. The recipient form includes the unique donor number, donor blood type (ABO and Rh) and name of the issuing technologist.

The circulating nurse confirms that the donor number on the allograft package matches the recipient form and relays information to the surgeon about blood type, Rh factor and use of Proviodine at the time of procurement.

The outer plastic wrap is opened by the circulating nurse and the bone is transferred to the sterile table. A small biopsy specimen is taken for culture (results are sent to bone bank). The bone is soaked in a warm (40°C) antibiotic solution of 80 mg tobramycin, 1 g cefazolin (Kefzol) and 50 000 U bacitracin per 1000 mL of Ringer's lactate solution for at least 10 minutes before use.

The completed recipient form includes recipient's name, identification number, diagnosis, surgeon's name, surgery performed and use of allograft bone. A copy may be maintained in the patient chart. If not, the unique donor number is recorded in the surgical report. The original recipient form is maintained in confidence by the bone bank. The bone bank also retains any reports of adverse reactions or problems.

Only femoral heads that have not been used and are promptly returned to the bone bank are considered acceptable for reuse. Any bone that has been exposed to the recipient operating field but not used, or has been used in part, is unacceptable.

An unused, returned bone graft is accompanied by a statement as to the course of the graft and the reason for return. Acceptance of this graft is determined by the bone-bank medical director.

Discussion

Donor Screening

Donors are typically patients who undergo total joint replacement for osteoarthritis or femoral-head fracture. They are otherwise healthy individuals, free of malignant disease (with the exception of primary basal cell tumour of skin following excision), absence of infection or history of communicable disease (Table I). Diseases of unknown etiology (rheumatoid arthritis, autoimmune diseases, systemic lupus erythematosus) and life-styles considered to be at high risk (intravenous drug abuse, recipients of clotting factor concentrate, sexual activity

at risk for AIDS) are also contraindications to donation.[18,26]

Complete screening of social and medical history cannot be overemphasized. A small but definite rate of false-negative results is possible with serologic testing, indicating that use of bone from patients in high-risk groups is not acceptable despite negative serologic results for HIV-1 and hepatitis B.[27] Serologic tests for many viruses that slowly affect nerves are not available; only a clinical observation of rapid dementia may indicate the presence of disease.[28] Age does not preclude the usefulness of the bone-graft material, but may make it more difficult to obtain an acceptable medical history and rule out disease-related dementia (e.g., Creutzfeldt–Jakob disease, Alzheimer's disease, rabies). No confused or demented patient should be accepted as an organ, blood or tissue donor.[29]

Currently there are no approved serologic tests for screening blood and tissue donors for non-A, non-B hepatitis (NANB).[30] Nonspecific means of screening against NANB include surrogate testing for HBcAb and screening with respect to the medical and social histories.[30,31] The American Red Cross now screens all blood donors for human T-cell lymphotrophic virus type I (HTLV-1).[32] This is not current practice in Canada since HTLV-1 has a lower prevalence in the general population, so that there is a greater chance of a false-positive result; also, the specificity of the test is low in Canadian subjects. A summary of current serologic tests and acceptable results is presented in Table II.

Screening for contraindications should be continued at the postoperative follow-up examination. Any clinical observations of swollen lymph nodes, prolonged high body temperature, infection or high leukocyte count should be noted. These may not be absolute contraindications but could be evidence of potential disease or infection.

Cultures

Swabs for culture are of minimal or no value.[33] Biopsy or curettage are better procedures. Specimens are transferred to the microbiology laboratory in dry sterile containers with appropriately marked requisitions. They should not be placed into liquid media. Specimens taken at time of procurement are labelled "Donor." A second specimen obtained at the time of implantation is labelled "Graft."

The bone chips or soft-tissue biopsy specimens are cultured in cooked meat broth at 37°C for 6 days. They are observed for growth over the incubation period. If growth is observed, or at day 6, the specimen is subcultured onto blood agar aerobically and BHI agar anaerobically at 37°C for 48 hours. All isolates from these specimens are considered pathogens, including diptheroids and coagulase-negative staphylococci. If growth is from the "Donor" specimen, only identification is required. If the growth is from the "Graft" specimen identification and susceptibility testing are carried out on each isolate. Records of culture results from all graft specimens are maintained to help provide a view to quality assurance of the bone-bank program.

Quarantine

The AATB standards[18] state that "tissues from all living donors shall be held in quarantine for at least 90-days at which time the donor shall be tested for human immunodeficiency virus (HIV) antibody. Only if tests are negative for HIV shall tissue be released for distribution." This quarantine is considered necessary in order to accommodate the window of time between exposure to the virus and production of antibodies.[34,35] Most published reports suggest that the majority of cases show positive serologic results for the HIV-1 antibody by 9 weeks.[36–40] Cohen and associates[41] estimated the risk of HIV-1 transmission by transfusion at 0.003% (30 per million). Ward and colleagues[34] estimated the risk of transmission of HIV-1 at 26 per million transfusions. A recent report by the American Red Cross[42] stated that the probability of exposure to the AIDS virus from the screened blood supply in the United States in 1987 was 1:156 000 (6 in 1 million). Our protocol calls for rescreening of the social and medical histories and review of the postoperative follow-up at the clinical interview at least 90 days after procurement of the femoral head. By providing a quarantine of 12 or more weeks before testing for the HIV-1 antibody, it should be possible to reduce the risk a further 99%.[37] The risk by comparison would be less than 30 in 100 million.

We believe that an increase of the quarantine period from 12 weeks to 24 weeks as is the case for reproductive tissues[19,26,43] is unwarranted when a documented protocol for screening of medical and social his-

Table II. Summary of Acceptable Results of Serologic Tests

Test	Acceptable result
HIV-1 antibody (EIA screen)	Negative
HBsAg	Negative
HBcAb	Negative
VDRL (syphilis)	Non-reactive
Rh factor	Positive/negative
Blood type	A/B/AB/O

EIA = Enzyme-linked immunosorbent assay, HBsAG = hepatitis B surface antigen, HBcAb = hepatitis B core antibody.

tory accompanies HIV-1 antibody testing more than 90 days after surgical procurement. This rationale is supported by the Federal Centre for AIDS and the Working Group on HIV Infection in Organ and Tissue Transplantation, Health and Welfare Canada (A.J. Clayton, W. Schlech: Personal communication 1990).

"Flag" Method

Our experience has shown that most surgeons forget to obtain written consent for donation of harvested bone before surgery. They usually remember during the course of the hip replacement. This problem, combined with the 90-day quarantine for postoperative HIV testing, has led us to the protocol of obtaining written consent and doing all serologic testing at least 90 days postoperatively at the clinical follow-up.

A large red sticker or "flag" (Fig. 2) was designed to be attached to the outer jacket of the patient file or chart and serves to remind the surgeon that the patient's femoral head has been stored in the freezer and that consent for use and for serologic testing must be obtained.

Each consent form is accompanied by stepwise instructions for the review of the donor's history and clinical follow-up against possible contraindications, by instructions to obtain consent and details of serologic tests to be obtained and by a note instructing the laboratory to send the results to the bone bank.

We believe this method of flagging can also be applied to patients followed in a private office or an outside clinic, if staff notification and instructions are appropriate. Our own clinic is now adapting this to the hospital computer system. When the patient comes to the clinic, the data sheet automatically includes a flag to request donation and perform screening.

Consent

Femoral head bone banks should adhere strictly to established guidelines for testing, reporting and confidentiality.[44,45] There should be no testing for the HIV antibody without informed, written consent.[32,37,46] The patient should be apprised of the nature of bone banking and the need for screening and serologic testing.

Consent must include permission for donation of the bone for transplant and for serologic testing. It must be obtained in writing and must name all the tests to be performed (AIDS, hepatitis, syphilis). It should also state that all results are kept confidential and that any abnormal results are forwarded to the patient's physician. It is the responsibility of the physician to interpret the results of the test for the patient.[38]

We have instituted a system of obtaining consent after the 90-day quarantine period. The patient usually does not have to consent to the removal of the femoral head, since this is implicit in the surgical procedure. After the 90-day quarantine is the most appropriate time for screening for HIV-1 antibody, and this test is pivotal to the use of the femoral head for bone grafting. Asking patients at this stage is ethical because the treatment has not changed as a result of taking the femoral head and will not change whether consent is given or not. We find that few patients refuse consent at this stage.

The result of our protocol is a one-step procedure providing the 90-day quarantine for AIDS testing with written consent. There is no potential complication of dilution due to transfusion of blood products during surgery.[47] This protocol has the advantage of providing review of the medical history against contraindications at two stages and allowing a review of the postoperative clinical course.

Packaging

Packaging of the femoral head in a plastic container and three freezer bags has a number of advantages: an aseptic barrier is provided; water loss due to cold storage is eliminated; the disposable plastic container allows easy handling and removal of the frozen bone at implantation; the bone may also be thawed in warm antibiotics and damage to the outer wrap from the sometimes sharp bony edges of the graft is prevented; at the time of use, the outer bag is opened by the circulating nurse and the bone, still packaged in the two inner bags, is presented to the scrub nurse. The extra inner bag allows for the possibility of error in opening the package.

The patient addressograph label placed on the package at the time of procurement contains all immediate information required for bone-bank processing. When the allograft is considered acceptable for implantation (after all results are reported) this label is removed and the individual donor number is attached.

A label (or accompanying leaflet) is also attached, stating that the serologic results of graft specimens were negative for HIV-1 antibody, HBsAg, HBcAb and syphilis. It also gives information about the blood type and Rh factor and use of Proviodine at time of procurement.

Bone-Graft Storage

Long-term storage of allograft bone requires cold storage at tem-

peratures below −60°C. This cold environment is below the eutectic point of bone[48] and is cold enough to inhibit the degradative enzyme activity of collagenases.[49] The freezer should be equipped with high-temperature alarm sensors and a chart recorder to verify maintenance of environment.[26] This system should be checked and the temperature documented weekly with a manual alcohol thermometer. Access is limited to bone-bank personnel to prevent loss of banked bone and potential use of bone that has not been released for transplant.

By providing a second smaller refrigerator or freezer for temporary storage, it is possible to maintain limited access to the bone freezer and allow bone to be stored in a holding location until the results of the initial 48-hour cultures are known. This system helps reduce the possibility of contamination of the bone freezer and allows retrieved femoral heads to be deposited by operating-room staff.

It is important to place acceptable bone grafts in a physically separated part of the freezer and to document the placement systematically; this reduces the possibility of removing a graft that has not been approved and facilitates inventory checks of available allograft bone.

Antibiotic Prophylaxis

The 10% Proviodine solution, in which the bone is soaked at the time of procurement, is used as an antiseptic, because antibiotics require an incubation period before they are effective. The bone is thawed with a solution of bacitracin with an aminoglycoside (tobramycin) and cephalosporin (Kefzol). It provides wide-spectrum antibiotic prophylaxis[50–53] against the major aerobic and anaerobic pathogens. This protocol is similar to that used with large, open, surgical wound procedures[54–56] and allograft bone applications.[57] Thawing of bone before use provides an effective incubation period for the antibiotics and also allows the washing out of the residual Proviodine from the graft. The antibiotic solution may be substituted for the initial soaking in Proviodine, if desired.

The patient should also be maintained on an appropriate antibiotic prophylactic regimen, directed against the common pathogens associated with all orthopedic procedures.[57] We currently use a third-generation cephalosporin.

Rh Status of Donor Bone

The Rh status of donor bone must be documented and the recipient's surgeon made aware.[58] This is most important with allograft procedures to Rh-negative women with potential childbearing years remaining, although anti-Rh(D) immunoglobulin therapy is possible.[59]

Record Keeping

A surprisingly large number of forms have to be completed to maintain quality control of surgical bone grafts (see Table III). Instructions for screening, procurement, consent, serologic testing and use of graft are required to standardize these procedures, especially when a variety of medical and nursing staff may be involved.

Documentation of screening, procurement, consent, culture and serology results are also necessary for complete and accurate records (Table III).[18,23,26] A section in the serologic and culture results form should also include documented approval for release of tissue by the bone-bank director.

Also required is a recipient form. This form may combine graft information (Rh factor, date of procurement, serologic tests) as well as a section to be completed at the time of grafting, documenting recipient information, use of the graft, the surgeon's name and a notice stating that any adverse reactions should be reported to the bone bank.[60] The recipient form may be in duplicate, one copy to remain in the patient's chart and the other returned to the bone bank.

If the recipient form cannot be included with the patient chart, the unique donor number is recorded on the operative report.

Use of a personal computer for database, inventory and word processing is ideal[61] to maintain accurate physical records, help with inventory, produce forms and tabulate incomplete serology and microbiology reports.

Personnel

Daily operations, record keeping and distribution of allografts may

Table III. Standardized Forms of Instruction and Documentation Required for Banking Bone From Surgical Donors

Form	Type	Description
FH1	Instruction	Screening and procurement instructions
FH2	Instruction	90-day postoperative screening, consent and serologic instructions
FH3	Instruction	Instructions for clinical application
FH4	Document	Procurement and screening documentation
FH5	Document	Witnessed consent form
FH6	Document	Record of testing and release signature
FH7	Document	Graft statement, recipient data and adverse reaction form

be performed by a designated technologist or operating-room staff member. Overall operation of the bone bank, release of acceptable tissues and verification of documented policies is the responsibility of the bone-bank medical director.[18]

Protocols are written and updated from recommendations made by clinicians, operating-room nursing staff and the departments of pathology and microbiology.

Conclusions

Standards for banking bone from surgical donors now include a 90-day quarantine, at which time the donor is tested for the HIV-1 antibody. This quarantine emphasizes the need for dedicated equipment and documented standards in donor selection, tissue recovery, preservation techniques, storage, record keeping and distribution.

The screening of medical and social histories, and serologic testing for HIV-1 antibody, HBsAg, HBcAb and syphilis after a 90-day quarantine minimize the risks of transmitting disease through the graft. This is a safe and effective program, which streamlines the paperwork and handling of banked surgical bone. The methodology described meets or exceeds criteria set by the Centers for Disease Control in Atlanta, the US Food and Drug Administration and the AATB.

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Addendum

Effective Aug. 1, 1990, The American Association of Tissue Banks (AATB) (as stated in its newsletter volume 13, number 3) requires that all tissue donors be screened for the antibody to the hepatitis C virus (HCV). Although questions have been raised as to the sensitivity and specificity of current tests, they are being applied in the screening of all volunteer blood donors by the American and Canadian Red Cross societies. A positive result from an HCV test would require that the banked tissue be discarded. Absence of a confirmatory antigen test necessitates the counselling of living donors about the possibility of being positive for HCV.

Future test kits may be of better benefit in screening HCV from those in non-high-risk groups. Meanwhile, this test will replace the hepatitis B core antibody (HBcAb) test described in our paper.

In a recent newsletter (volume 13, no. 4, 1990) the AATB stated that, effective Apr. 1, 1991, an increase in the quarantine will be required for surgical bone donors, from 90 to 180 days. After that time the donor is to be screened for human immunodeficiency (HIV-1) and HCV antibodies.

This increase in the quarantine appears to be in response to the possibility of long-delayed seroconversion and brings surgical bone donation in line with banking of reproductive tissues from living donors. In our view, as described in detail in our paper, this increase in quarantine may not add any substantial benefit in terms of reducing the risk of HIV-1 transmission. It may even make the banking of surgical bone less feasible and result in more orthopedic practices opting for cadaveric bone banking, for which there is no option for quarantine and no way of accounting for the window of time between exposure and seroconversion.

In the banking of human tissue for clinical transplantation there will always be improvements to protocols and screening criteria. The value of these new applications should be weighed with consideration given to the prevalence of cases at risk in the donor population and the increased costs of application.■

When choosing an antibiotic for nosocomial infections,

LOOK BEYOND THE PRICE TAG.

Look at the safety profile and total cost of treatment.

Significant biliary excretion of antibiotics can have a very disruptive effect on intestinal flora, which may promote the emergence of resistant strains of bacteria and cause diarrhea.[1,2] This can add substantially to the cost of treatment.[3]

CLAFORAN (cefotaxime sodium) has an excellent safety profile. With only 5% biliary excretion, Claforan has little effect on intestinal flora, thus reducing the risk of diarrhea and bacterial resistance.[1,4] And Claforan provides excellent coverage of major nosocomial pathogens.

Over a complete course of therapy, if one looks at the average cost per patient, Claforan makes good sense.[5]

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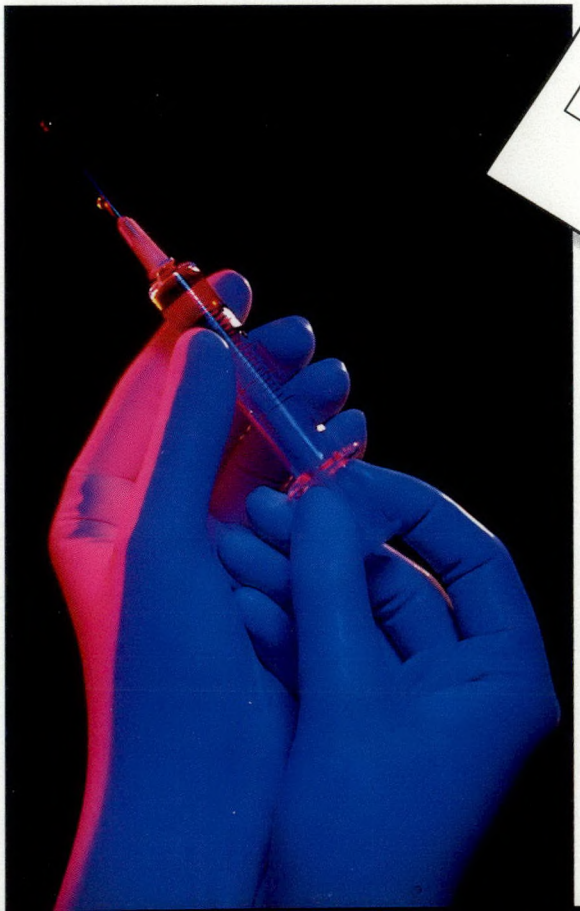

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PRESCRIBING INFORMATION

Action

In vitro studies indicate that the bacterial action of Claforan (cefotaxime sodium) a semi-synthetic cephalosporin antibiotic, results from inhibition of cell wall synthesis.

Indications and Clinical Uses

Treatment : Claforan (cefotaxime sodium) may be indicated for the treatment of infections caused by susceptible strains of the designated micro-organisms in the diseases listed below.

Lower respiratory tract infections : pneumonia and lung abscess caused by *Streptococcus pneumoniae* (formerly *Diplococcus pneumoniae*), other streptococci (excluding enterocci, e.g. *S. faecalis*), *Straphylococcus aureus* (penicillinase and non-penicillinase producing), *Escherichia coli*, *Hemophilus influenzae*, (including ampicillin resistant strains) and unspecified *Klebsiella* species.

Urinary tract infections : caused by *Escherichia coli*, unspecified *Klebsiella* species (including *K. pneumoniae*), *Proteus mirabilis*, indole positive *Proteus*, *Serratia marcescens* and *Staphylococcus epidermidis*. Also, uncomplicated gonorrhea caused by *N. gonorrhoeae* including penicillin resistant strains.

Bacteremia / Septicemia : caused by *Escherichia coli*, unspecified *Klebsiella* strains and *Serratia marcescens*.

Skin infections : caused by *Staphylococcus aureus* (penicillinase and non-penicillinase producing, *S. epidermidis*, Group A streptococci, *Escherichia coli*, *Proteus mirabilis* and indole positive *Proteus*.

Intra-abdominal infections : caused by *Escherichia coli*, and unspecified *Klebsiella* species.

Gynecological infections : including pelvic inflammatory disease, endometritis and pelvic cellulitis caused by *E. coli*, Group A streptococci and *Staphylococcus epidermidis*; anaerobic bacteria including unspecified *Peptococcus* and *Peptostreptococcus* strains and some strains of *Bacteroides fragilis*. In several cases, although clinical cures were achieved, bacteriological follow-up was not available.

Central nervous system infections : meningitis and ventriculitis caused by *Haemophilus influenzae*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae* and *Escherichia coli*. Claforan is not active against *Listeria monocytogenes*.

Clinical experience with Claforan in anaerobic infections is limited. Claforan has been used with some success in wound and intra-abdominal infections against some strains of unidentified *Bacteroides* and anaerobic cocci.

Claforan has been shown to be active against some strains of *Pseudomonas*.

In the treatment of infections encountered in immunosuppressed and granulocytopenic patients, results of therapy with Claforan have not been impressive.

Claforan should not be considered in the treatment of enterococcal infections, i.e. *Streptococcus faecalis*.

Specimens for bacteriologic culture should be obtained prior to therapy in order to isolate and identify the causative organisms and to determine their susceptibilities to Claforan. Therapy may be instituted before results of susceptibility studies are known; antibiotic treatment should be re-evaluated once these results become available.

Prophylactic Use : The administration of Claforan perioperatively (preoperatively, intraoperatively and postoperatively) may reduce the incidence of certain infections in patients undergoing elective surgical procedures (e.g. abdominal or vaginal hysterectomy, gastrointestinal and genitourinary tract surgery) that may be classified as contaminated or potentially contaminated.

In patients undergoing caesarian section who are considered to be at increased risk of infection, intraoperative (after clamping the umbilical cord) and postoperative use of Claforan may also reduce the incidence of certain postoperative infections.

Effective use for elective surgery depends on the time of administration (see Dosage and Administration).

For patients undergoing gastrointestinal surgery, preoperative bowel preparation by mechanical cleansing as well as with a non-absorbable antibiotic (e.g. neomycin) is recommended.

If there are signs of infection, specimens for culture should be obtained for identification of the causative organism so that appropriate therapy may be instituted.

Contraindications

Claforan is contraindicated in patients who have shown hypersensitivity to cefotaxime sodium, the cephalosporin or the penicillin groups of antibiotics.

Warnings

Before therapy with Claforan is instituted, it must be carefully determined whether the patient has had previous hypersensitivity reactions to cefotaxime, cephalosporins, penicillins or other drugs. Claforan should be given with caution to patients with Type 1 hypersensitivity reactions to penicillin. Antibiotics, including Claforan should be administered with caution to any patient who has demonstrated some form of allergy, particularly to drugs. If an allergic reaction to Claforan occurs, the drug should be discontinued and the patient treated with the usual agents (e.g. epinephrine, antihistamine, pressor-amines or corticosteroids).

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad spectrum antibiotics); therefore, it is important to consider its diagnosis in patients who develop diarrhea during the administration of Claforan. This colitis can range from mild to life-threatening in severity.

Treatment with broad spectrum antibiotics, such as Claforan, alters the normal flora of the colon and may permit overgrowth of *Clostridium difficile* or other clostridia. It has been established that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of colitis may respond to discontinuation of Claforan and replacement with a suitable specific antibiotic. Moderate to severe cases should be managed with fluid, electrolyte and protein supplemntation as indicated.

When the colitis is not relieved by discontinuance of Claforan administration or when it is severe, an antibiotic specifically effective in antibiotic-associated pseudomembranous colitis (e.g. vancomycin) or other suitable therapy may be indicated. Other possible causes of colitis should also be considered (see Adverse Reactions).

Precautions

Claforan (cefotaxime sodium) should be prescribed with cauton in individuals with a history of lower gastro-intestinal disease, particularly colitis.

The safety of Claforan in pregnancy has not been established. Consequently, use of the drug in pregnant women requires that the likely benefit from the drug be weighed against the possible risk to the mother and fetus.

Use of Claforan in women of child-bearing potential requires that the anticipated benefits be weighed against the possible risks.

Cefotaxime is excreted in human milk in low concentrations. Caution should be exercised when the drug is administered to nursing mothers.

Prolonged use of Claforan may result in the overgrowth of nonsusceptible organisms. Constant evaluation of the patient's condition is essential. If super-infection occurs, therapy should be discontinued and appropriate measures taken.

Although Claforan rarely produces alterations in kidney function, evaluation of renal status is recommended, especially in severely ill patients receiving high doses.

Patients with markedly impaired renal function should be placed on the special dosage schedule recommended under Dosage and Administration, because normal dosage in these individuals is likely to produce excessive and prolonged serum antibiotic concentrations.

Positive direct Coomb's test is known to develop in individuals during treatment with the cephalosporin group of antibiotics, including cefotaxime sodium.

In laboratory tests a falso positive reaction to glucose may occur with reducing substances but not with the use of specific glucose oxidase methods.

Adverse Reactions

The most frequent adverse reactions with their frequency of occurrence are :

Hypersensitivity (1.8%) : Rash, pruritus, fever. Local (5%) : Injection site inflammation with intravenous administration. Pain, induration and tenderness after intramuscular injection. Gastrointestinal (1.7%) : Colitis, diarrhea, nausea and vomiting. Symptoms of pseudomembranous colitis can appear during or after Claforan treatment. Hemic and Lymphatic System (< 1%) : Mild, reversible leukopenia, granulocytopenia and thrombocytopenia have been reported. Some patients developed positive direct Coomb's test during treatment with Claforan. Genitourinary System (< 1%) : Moniliasis, vaginitis. Liver (< 1%) : Transient elevations in SGOT, SGPT, serum LDH and serum alkaline phsphatase levels have been reported. Kidney (< 1%) : Increased serum creatinine and BUN have occasionally been observed. Central Nervous System (0.2%) : Headache.

Symptoms and Treatment of Overdosage

Since no case of overdosage has been reported to date with Claforan, no specific information on symptoms or treatment is available. Treatment of overdosage should be symptomatic.

Dosage and Administration

Claforan (cefotaxime sodium) may be administered intramuscularly or intravenously after reconstitution (see Table with recommended mode of reconstitution according to route of administration).

Adults

The dosage of Claforan should be determined by susceptibility of the causative organisms, severity of the infection and condition of the patient.

Guidelines for Dosage of Claforan (cefotaxime sodium)

Type of Infection	Daily Dose (g)	Frequency and Route
Uncomplicated Gonorrhea	1	1 g IM (single dose)
Uncomplicated infections	2	1 g every 12 hours IM or IV
Moderately severe to severe infections	3-6	1-2 g every 8 hours IM or IV
Very severe infections (e.g. septicemia, CNS)	6-8	2 g every 6-8 hours IV
Life-threatening infections	up to 12	2 g every 4 hours IV

To prevent postoperative infection in contaminated or potentially contaminated surgery, recommended doses are as follows.

(a) 1 g IM or IV administered 1/2 to 1-1/2 hours prior to the initial surgical incision to ensure that adequate antibiotic levels are present in the serum and tissues at the start of surgery

(b) 1 g IM or IV administered 1-1/2 to 2 hours following the first dose; for lengthy operative procedures, additional intraoperative doses may be administered, if necessary, at appropriate intervals (1-1/2 to 2 hours) during surgery

(c) 1 g IM or IV administered within 2 hours following completion of surgery

The total cumulative prophylactic dose should not exceed 6 g in a 12 hour period.

Caesarian Section Patients

The first dose of 1 g is administered IV as soon as the umbilical cord is clamped. The second and third doses should be given as 1 g IM or IV at 6 and 12 hours after the first dose.

Neonates, Infants, and Children

The following dosage schedule is recommended :

Neonates :	0-1 week of age	50 mg / kg IV q 12 h
	1-4 weeks of age	50 mg / kg IV q 8 h

Infants and children (1 month to 12 years) : For body weights less than 50 kg, the recommended daily dose is 50 to 100 mg / kg IM or IV of body weight divided into 4 to 6 equal doses, or up to 180 mg / kg / day for severe infections (including central nervous system infections).

For body weights 50 kg or more, the usual adult dosage should be used.

The maximum daily dosage should not exceed 12 grams.

Administration of Claforan should be continued for a minimum of 48 to 72 hours after the patient defervesces or after evidence of bacterial eradication has been obtained; a minimum of 10 days of treatment is recommended for infections caused by Group A beta-hemolytic streptococci in order to guard against the risk of rheumatic fever or glomerulonephritis; frequent bacteriologic and clinical appraisal is necessary during therapy of chronic urinary tract infections and may be required for several months after therapy has been completed; persistent infections may require prolonged treatment. Doses less than those recommended should not be employed.

Dosage for Patients with Impaired Renal Function

In patients with estimated creatinine clearance of less than 20 mL / min / 1.73m^2 the dose of Claforan should be halved (see Precautions).

If serum creatinine values alone are available, the following formula (based on sex, weight, and age of the patient) may be used to convert these values into creatinine clearance.

Males : $\dfrac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine}}$

Females : $0.85 \times$ above value

Administration

Intramuscular : Claforan should be injected well within the body of a relatively large muscle such as the upper outer quadrant of the buttock (i.e. gluteus maximus); aspiration is necessary to avoid inadvertent injection into a blood vessel.

Intravenous : The intravenous route is preferable for patients with bacteremia, bacterial spticemia, or other severe or life-threatening infections, or for patients who may be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or impending.

For bolus administration a solution containing 1 or 2 g of Claforan can be injected over a period of 3 to 5 minutes. Using an infusion system, it may also be given over a longer period of time through the tubing system by which the patient may be receiving other intravenous solutions. Butterfly* or scalp vein type needles are preferred for this type of infusion. However, during infusion of the solution containing Claforan, it is advisable to discontinue temporarily the administration of other solutions at the same site.

ADD-Vantage* Vial

When administering Claforan using the ADD-Vantage* Drug Delivery system, Claforan powder is added directly to a single-dose flexible plastic ADD-Vantage* diluent container. Claforan 1 g or 2 g may be reconstituted in 50 mL or 100 mL of 5% Dextrose Injection USP or 0.9% Sodium Chloride Injection USP.

Stability

Solutions of Claforan reconstituted in 5% Dextrose Injection USP or 0.9% Sodium Chloride Injection USP in the ADD-Vantage* flexible containers maintain satisfactory potency for 12 hours at room temperature.

Availability

Claforan (cefotaxime sodium) is supplied as a sterile, white to pale yellow powder, in vials containing 500 mg, 1.0 and 2.0 g of cefotaxime sodium and in ADD-Vantage* vials containing 1.0 and 2.0 g of cefotaxime sodium (expressed as acid on a dry basis).

Storage : Claforan in the dry state should be stored at room temperature protected from light and heat.

Product monograph available on request.

*Reg'd TM of Abbott Laboratories.

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Comparison Between Patellar Resurfacing With an Inset Plastic Button and Patelloplasty

H.U. Cameron, MB, ChB, FRCSC*

Of 101 patients who underwent knee replacement with the Tricon P prosthesis and were followed up for 2 or more years, 68 had patellar resurfacing with a recessed press-fit plastic button and 43 patients had patelloplasty (shaving of the patella and removal of osteophytes). All patients were followed up for more than 2 years.

Three percent of the patients who had patellar resurfacing, later had patellar fractures; 4.6% of the patients who had patelloplasty initially, subsequently required patellar replacement. There were no instances of loosening of the patellar replacement.

Patellofemoral aching was experienced by 7.6% of the patients who had patellar resurfacing and by 17.6% of those who did not. Of the patients who had patellar resurfacing, 61.5% could climb stairs without aids using the replaced side as the lead leg compared with 37.2% of the patients who had patelloplasty. Overall ratings of the surgical results were similar for the two groups.

The author concludes that patellar resurfacing improves the quality of the result and that there are few drawbacks to the use of an inset patellar button.

Sur 101 patients qui reçurent une prothèse du genou de type Tricon P et qui furent suivis pendant 2 ans ou plus, 68 avaient eu une mise à neuf de la surface rotulienne à l'aide d'un bouton de plastique appareillé par pression alors que les 43 autres avaient subi une plastie de la rotule (planage de la rotule et enlèvement des ostéophytes).

Trois pourcent des patients qui avaient eu une remise à neuf de la surface rotulienne, subirent plus tard une fracture; 4.6% des patients qui avaient eu une plastie de la rotule nécessitèrent par la suite le remplacement de celle-ci. On n'a constaté aucun détachement de prothèse.

Des douleurs rotulo-fémorales ont été rapportées par 7.6% des patients qui avaient eu une remise à neuf de la surface et par 17.6% de ceux qui n'en avaient pas eu. Des patients qui avaient eu une remise à neuf de la surface rotulienne, 61.5% pouvaient monter un escalier sans aide en utilisant le côté opéré comme jambe d'appui, comparativement à 37.2% pour ceux qui avaient une plastie rotulienne. L'évaluation globale des résultats chirurgicaux a été la même pour les deux groupes.

L'auteur conclut que la remise à neuf de la surface rotulienne améliore la qualité des résultats et qu'il y a peu d'inconvénients à utiliser un bouton de plastique incrusté dans la rotule.

From the Department of Surgery, The Orthopaedic and Arthritic Hospital, University of Toronto, Toronto

**Assistant professor, Department of Surgery, Department of Pathology and Department of Engineering, University of Toronto. Staff orthopedic surgeon, The Orthopaedic and Arthritic Hospital, Toronto*

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Reprint requests to: Dr. H.U. Cameron, Ste. 318, 43 Wellesley St. E, Toronto, ON M4Y 1H1

Problems resulting from the use of metal-backed patellar prostheses[1,2] have led to doubt about the value of patellar replacement. In an attempt to define the advantages and disadvantages of patellar replacement, I compared two groups of patients who received a Tricon P knee replacement; one group had patellar resurfacing, the other did not.

The Tricon P knee prosthesis (Richards Manufacturing Co., Memphis, Tenn.) was introduced in 1982. A refinement of the RMC knee prosthesis,[3] it consisted of a cemented femoral component and uncemented tibial and patellar components. The tibial component was held in place by ridged plastic pegs[4] driven into undersized holes drilled into the centre of the medial and lateral tibial plateaus. Although these plastic pegs lasted reasonably well,[5] for long-term fixation, undercut grooves were machined into the undersurface of the tibial component to allow for possible bone upgrowth (Fig. 1).

The Tricon P patellar component is a plastic button with a central peg. It is inserted by reaming an exact-sized hole into the centre of the patella and press-fitting the component without cement (Fig. 2). Recession of this component allows the shear loads on the patella to be absorbed by the side walls of the component and not the central peg. The component is load-sharing in the sense that most of the contact between the patella and the metallic

trochlear groove occurs on the plastic insert, but some bony contact around the periphery is possible.

At first the advantages of a patellar component were not obvious and it was seldom used. Later, however, it was used universally. All patellar components were inserted without cement.

Methods

One hundred and one patients who underwent knee replacement with the Tricon P prosthesis between 1982 and 1987 at the Orthopaedic and Arthritic Hospital in Toronto, and who were followed up for 2 or more years, were reviewed prospectively according to the Hospital for Special Surgery rating system.[6] Follow-up was at 3 months and 6 months after placement and annually thereafter. At each visit, 1-m standing anteroposterior, lateral and skyline x-ray films were obtained.

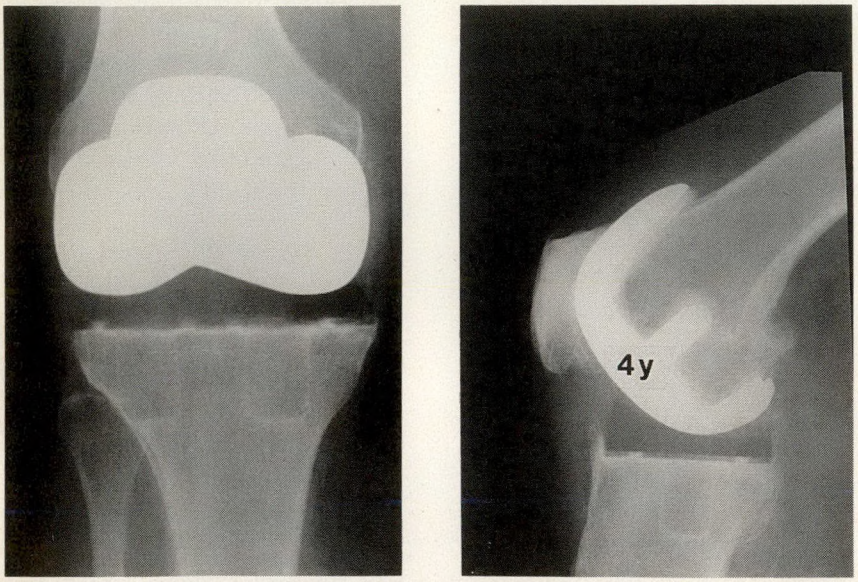

FIG. 1. Tricon P replacement knee, showing grooves and flanges in two Freeman pegs that hold implant in place. Undercut grooves have filled with bone and have upside-down triangular shape, indicating that this bone is not produced by sinkage. Patella has not been replaced in this case.

Technique

In all cases a midline skin incision was made. Early in the series the knee was opened with a lateral parapatellar capsular incision to avoid patellar avascular necrosis.[7] Later a medial parapatellar capsular incision was used if the patella was located centrally, and a lateral approach was used only if the patella was in a laterally subluxed position preoperatively.

The upper surface of the tibia was cut off at right angles to the floor using an extramedullary guide, and holes were drilled in the centre of the lateral and medial tibial plateaus to receive the pegs. Ligaments were balanced by means of lamina spreaders. The distal femoral condyles were cut with an intramedullary guide set at 7° of valgus. The amount of distal femoral resection matched the thickness of the metal component so as to prevent proximal shift of the joint line.[3] The anterior and posterior femoral condyles were resected, removing the same minimal amount of bone from both posterior femoral condyles to ensure that the knee would be tight in flexion.[8] Initially the posterior cruciate ligament was completely resected, but later in the series it was simply left, or, if it was tight, a midsubstance step cut was made. Initially the patella was

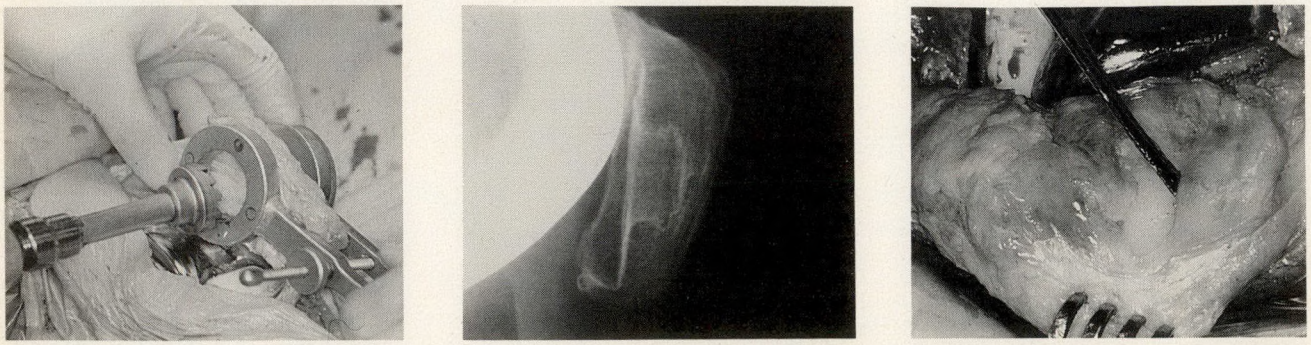

FIG. 2. (Left) Patella is grasped in holder and central hole reamed out. (Middle) Close-up view shows outline of recessed patella and fixation peg. Walls of plastic patella are surrounded by bone. (Right) Typical fibrous meniscus that surrounds and overgrows patellar button.

shaved and the osteophytes were removed; later in the series routine patellar replacement was carried out using the press-fit patellar component already described.

All femoral components were cemented in place. Cement was used to hold the tibial component in place only if the bone was unusually soft (if it could readily be indented by finger pressure) or if substantial bone loss had occurred; these conditions were more common in patients who underwent revisions of previous surgical procedures. Apart from these indications, all tibial components were inserted without cement. Later in the series tibial defects were repaired by bone grafting.[9] Unless the tibial bone grafts were large, all patients were allowed immediate full weight bearing. The patients considered in this study all had noncemented tibial components.

Findings

Patellar Resurfacing

Sixty-eight patients (9 men 59 women, mean age 71 years) underwent patellar resurfacing. The follow-up ranged from 2 to 5 years (mean 3.5 years). Three of these patients underwent revision of previous surgery and are considered separately.

The results in 39 (60%) patients were rated as excellent, in 23 (35.4%) as good and in 3 (4.6%) as fair. Only five (7.6%) patients complained of aching in the patellofemoral joint during use. Forty (61.5%) patients could climb stairs with no aids using the operated leg as the lead leg; 15 (24%) patients needed the assistance of a handrail to use the operated leg as the lead leg when climbing stairs and 10 (15%) used the other leg.

One of the three patients who required revision of a previous surgical procedure experienced a supracondylar fracture 2 years after operation. Open reduction and internal fixation were carried out. The femoral component subsequently loosened and required revision. The second patient had loosening of the femoral component at 3 years. At revision the tibial component was found to be tight. The third patient required a revision operation at 3 years to repair a sunken tibial component. The medial tibial plateau had fractured before surgery and had been inadequately reconstructed.

One man continued to have patellofemoral pain. His patella was revised to a metal-backed patella at 1 year. He continued to have some patellar aching, and his patella was again revised, 4 years later, to a custom-made patellar component that covered the whole surface of the patella. Currently he is doing well. Two patients had neuroma of the infrapatellar branch of the saphenous nerve, which took 18 months to settle, and three patients had a minor wound dehiscence of no particular significance. Two patients (3%) had a patellar fracture. One fracture occurred at 10 months in a patient in whom a lateral parapatellar approach had been used. The fracture, which was transverse with no separation, healed with a fibrous nonunion. The other, a longitudinal fracture at 18 months, occurred in a patient who had had a medial incision with no lateral release. Both patients were treated simply by bracing for 4 weeks.

Patelloplasty

This group comprised 43 patients (6 men 37 women, mean age 72 years). The follow-up ranged from 2 to 7 years (mean 4.5 years). Twenty-seven patients had the opposite knee replaced with some other type of prosthesis, and 5 patients had other joints replaced.

In this group the results were rated as excellent in 25 (58.1%) patients, good in 15 (34.9%) patients and fair in 3 (7%) patients. Seven (16.2%) patients complained of patellofemoral aching. Sixteen (37.2%) patients could use the operated leg as the lead leg when climbing stairs without using aids. Nine patients (20.9%) could use the operated leg as the lead leg if they used the handrail and 18 (41.9%) patients used the opposite leg as the lead leg for stair-climbing.

None of the patients in this group required surgical revision. Two patients required patellar resurfacing to relieve significant patellofemoral pain, one at 14 months and one at 19 months.

Discussion

In this study group the only patellar problems potentially related to patellar resurfacing were two fractures (3%). Of those who did not have their patellas resurfaced, 4.6% subsequently required resurfacing. Patellofemoral ache was present in 16.2% of those with no resurfacing and in 7.6% of those who had resurfacing. When climbing stairs, 61.5% of the patients who underwent patellar resurfacing could ascend without aids, using the leg with the replaced knee as the lead leg, compared with 37.2% of those who did not undergo resurfacing. There were minimal differences in the ratings between the two groups: the results of 95.4% of the group with patellar resurfacing were rated as good or excellent compared with 93% of the group with patelloplasty.

It is obvious therefore that resurfacing the patella seldom influences the overall result but does affect the

quality of the results. The knee rating systems are coarse instruments at best and are not capable of reflecting subtle differences, although stair-climbing ability differed markedly between the two groups.

The recessed plastic press-fit patella has functioned well. The knees that have been revised have generally shown wear only on a single central facet, in spite of an average range of motion greater than 100°. The recession coupled with the development of a fibrous patellar meniscus[10] presumably protects the components. No loosening and no subsidence into the patella have been noted, all components being surrounded by a peri-implant bone plate. There must be some concern that, with time, there will be a build-up of polyethylene debris from this interface, possibly leading to late bone resorption and loosening,[11] but this has yet to be seen. Use of a lateral or medial parapatellar approach does not seem to influence the result, and at our institution we continue to use a medial parapatellar incision when the patella is situated centrally before surgery and a lateral approach when it is subluxed laterally.

The results of this study indicate that the drawbacks to resurfacing the patella are minimal and that the improvement in "quality of life" for patients who undergo this procedure is significant.

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Reviewers 1990

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Etiology of Prosthetic Anastomotic False Aneurysms: Pathologic and Structural Evaluation in 26 Cases

A.R. Downs, MD;*† R. Guzman, MD;*† M. Formichi, MD;* R. Courbier, MD;‡ J.M. Jausseran, MD;‡ A. Branchereau, MD;¶ C. Juhan, MD;§ N. Chakfe, MD;* M. King, PEng;** R. Guidoin, PhD*

To determine the etiology of anastomotic false aneurysms (AFAs), 26 textile graft specimens, removed because of AFA, were studied morphologically, histologically and by scanning electron microscopy. No cases of suture-related failures leading to AFA were found. Nine cases of frayed grafts were documented but were not the cause of AFA formation. In three cases, chemical degradation of the fibres, which may have been secondary to lipid infiltration, may have contributed to AFA formation. There were no cases of overt clinical infection, but the presence of bacteria was documented by scanning electron microscopy in 20 cases. The role of bacteria is not well defined, but they may be a factor in host arterial-wall degeneration as a cause for AFA formation.

L'étiologie des faux anévrismes a été étudiée à l'aide de 26 segments prothétiques en polyester, explantés pour résection de faux anévrismes et analysés macroscopiquement, en microscopie optique et en microscopie électronique à balayage. Aucun cas de rupture de suture n'a été noté. Neuf segments prothétiques présentaient un effilochage à leur extrémité, mais celui-ci n'était pas responsable de la formation des faux anévrismes. Cependant, parmi les défaillances prothétiques ayant pu contribuer à la formation des faux anévrismes, nous avons observé trois cas de dégradation chimique des fibres vraisemblablement secondaire à une infiltration de lipides. Parmi les spécimens étudiés, nous n'avions aucun cas d'infection clinique, cependant une colonisation bactérienne a été observée en microscopie électronique à balayage dans 20 cas. Le rôle des bactéries doit être élucidé et il pourrait agir comme facteur de dégénérescence de la paroi artérielle responsable de la formation de faux anévrismes.

*Biomaterials Institute, St-François d'Assise Hospital and Laboratory of Experimental Surgery, Laval University, Quebec

†Section of Vascular Surgery, Health Sciences Centre, University of Manitoba, Winnipeg

‡Service de chirurgie cardiovasculaire, Hôpital St-Joseph, Marseille, France

¶Service de chirurgie vasculaire, Groupe hospitalier de la Timone, Marseille

§Chirurgie vasculaire, Hôpital Nord, Marseille

**Department of Clothing and Textiles, University of Manitoba, Winnipeg

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Reprint requests to: Dr. Robert Guidoin, Biomaterials Institute F1-304, St-François d'Assise Hospital, Quebec, PQ G1L 3L5

Anastomotic false aneurysms (AFAs) at the junction of prosthetic arterial anastomoses continue to be a relatively common late complication of grafting.[1] The etiology of AFA is multifactorial. The recognized causes include suture dissolution or fracture, overt infection at the anastomosis, dilatation of the graft, rupture of the prosthesis and fraying of the prosthesis at the suture line. Predisposing factors considered to play a role are endarterectomy near the anastomotic site, compliance mismatch between the prosthesis and the artery, inappropriate graft–arterial diameter ratio, repeated mechanical traction at the anastomosis and shortening of the graft.[2] The most common finding at the site of the anastomosis in the noninfected false aneurysm is an intact suture line in the prosthesis pulled out from the arterial wall, usually at the toe of the graft. Sometimes the graft is completely separated from the artery. This finding has been attributed to the degeneration of the arterial wall at the anastomotic site,[3] but the cause or nature of the arterial-wall degeneration has not been elucidated. In an attempt to understand further the etiology of AFAs, 26 grafts that were resected at operation for AFA were submitted for gross morphologic and histologic investigation and scanning electron microscopy (SEM).

Patient Data and Methods

Twenty-six grafts, resected because of AFA over an 8-year period (1978 to 1986), were submitted for pathological investigation. All were removed by vascular surgeons in Marseille, France. An accompanying patient questionnaire, filled out by the attending surgeon, provided the relevant patient data. At the time of graft implantation the 23 men and 3 women ranged in age from 28 to 74 years (average 56.2 years). Indications for implantation were aortic occlusive disease in 23 patients and abdominal aortic aneurysm in 3 patients. The initial operative procedures performed are listed in Table I. Twenty-four repeat operations were performed because of a pulsatile mass in the groin (Table II) and the remaining 2 because of thrombosis of the graft. There was no clinical evidence of graft infection. At operation, a segment of graft was removed, and a short interposition graft was used to restore blood flow. No recurrences or infections were noted postoperatively at follow-up.

Processing of Graft Specimens

After excision, the grafts were opened longitudinally, carefully rinsed with heparinized saline, fixed in a buffered solution of 1.5% glutaraldehyde and shipped to the Biomaterials Institute at the St-François d'Assise Hospital in Quebec.

As part of the ongoing graft retrieval program, each specimen was processed through a series of pathological investigations. The graft specimen, including suture, was examined and photographed with a Tessovar macrophotography optical system (Carl Zeiss, Oberkochen, Germany). An appropriate representative segment was then selected for the pathological studies. Each segment was divided into two. The first piece was post-fixed in Perfix solution, dehydrated with ethanol and clarified with toluene before being mounted in paraffin. Sections 4 μm thick were then stained for light microscopy using Weigert's, Masson's trichrome and Gram's stains.

The second piece was post-fixed in thiocarbohydrazide and osmium tetroxide for examination by SEM. Dehydration was obtained by immersion in a series of ethanol solutions of increasing concentrations, culminating in pure ethanol, followed by critical-point drying with liquid carbon dioxide as the transfer medium. The specimen was then coated with gold–palladium and examined in a JSM 35CF scanning electron microscope (Jeol [USA] Inc., Peabody, Mass.) at 15 to 20 kV of accelerating voltage. The remaining graft specimens were cleaned for assessment of the textile material through a series of 5% sodium bicarbonate baths; this was followed by rinsing with distilled water.

Assessment Criteria

The sutures were assessed for type and for evidence of fractures or dissolution. The grafts were assessed for the following: type (macroscopically and by SEM), fraying (macroscopically and by SEM), fibre degradation (macroscopically and by SEM), lipid infiltration (macroscopically and by SEM), endothelialization (by SEM), integrity of the inner capsule and fibrin deposition (by SEM) and the presence of bacteria (histologically and by SEM).

Findings

The duration of implantation averaged 6.7 years (range from 1 to 10 years). Only five aneurysms were diagnosed within 5 years of implantation; the remaining 21 appeared between 5 and 10 years (Fig. 1).

The suture material used for the anastomosis was identified in all but four specimens. In 17 specimens, monofilament suture (Prolene) had been used, and in the remaining 5 specimens multifilament braided suture had been used. No suture fractures or dissolution was identified.

With respect to the types of grafts recovered at reoperation (Table III), no clustering of a single graft type within a given time period was demonstrated.

Fraying, seen in nine grafts, was most marked in the single woven graft submitted (Fig. 2). The presence of fraying did not seem to contribute to the formation of AFA in any case of this series.

Defects in the graft wall associated with chemical fibre degradation were seen in three grafts (Figs. 3 to 5). Lipid infiltration was seen in 17 grafts, the most marked being in a patient with hyperlipidemia.

Only one specimen had some evidence of endothelial cell growth, which was found near the anastomosis. In only 3 specimens was the integrity of the inner capsule composed of packed fibrin found to be

Table I. Types of Revascularization Procedures Performed on 26 Patients Who Had Grafts Removed Because of Aortic False Aneurysms

Procedure	Number of patients
Aortofemoral bypass	14
Unilateral aortofemoral or ileofemoral bypass	6
Femoropopliteal bypass	3
Axillofemoral bypass	1
Patch grafts (1 aortic, 1 iliac)	2

Table II. Site of Aortic False Aneurysms in 26 Patients

Site	Number of patients
Femoral	20
Popliteal	2
Aortic	3
Iliac	1

intact and confluent; in the remaining 23 specimens disrupted surfaces were demonstrated with patchy (15) or absent (8) internal capsules. Confluent and disrupted internal capsules are compared in Figs. 6 and 7 respectively.

In 18 specimens stained with Gram's stain, bacteria were not demonstrated; however, SEM demonstrated bacteria in 15 of these 18 specimens (Fig. 8). Overall, the presence of a discrete bacteremic colonization was demonstrated by SEM in 20 of 26 patients. No infection was detected clinically.

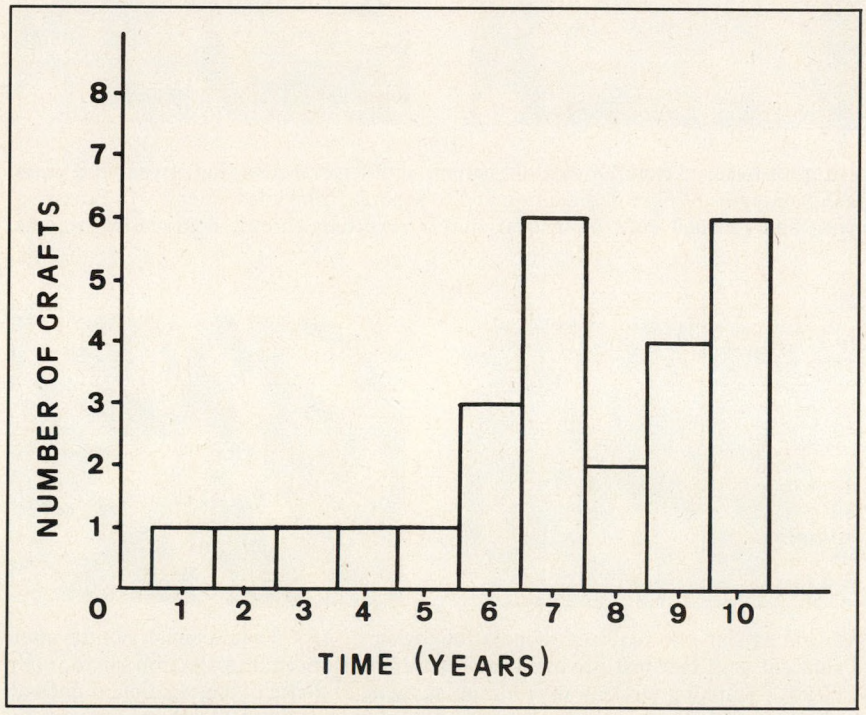

FIG. 1. Duration of function of 26 grafts before appearance of AFA.

Discussion

The etiology of AFA is multifactorial and can generally be classified into three major groups: suture fractures or dissolution, graft-related defects and factors related to the host artery or arterial–prosthetic junction.[4,5]

Currently, suture-related defects account for only a small proportion of all AFAs.[1-3] With the elimination of silk sutures and the more widespread use of nonabsorbable mono- or multifilament suture, reports of AFAs secondary to this group have diminished but have not been completely eliminated.[2,3,6] There were no suture-related failures leading to AFA formation in our series, which is consistent with this diminished trend.[4,5]

Graft-related defects again accounted for a relatively minor proportion of recognized causes of

Table III. Types of Grafts Used

Graft type	Number of patients
Weft knit flat fibre	7
Weft knit texturized fibre	9
Weft knit lightweight	3
Warp knit	5
Woven	1
Double velour	1

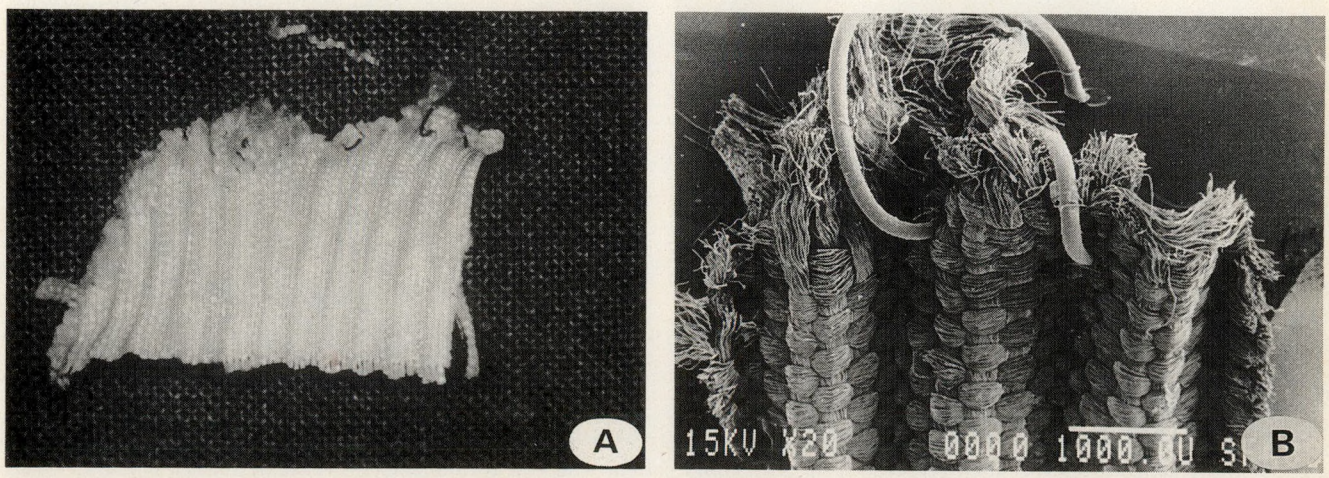

FIG. 2. (A) Cleaned graft specimen demonstrating fraying at edges of woven graft. (B) Scanning electron micrograph of frayed edges of graft (original magnification × 20).

AFA.[2,3,5] In this series, nine cases of fraying and three cases of fibre degradation were documented. Fraying did not lead to AFA in any case. However, the three cases of fibre degradation are of particular concern and likely contributed to AFA formation in two instances. Lipids may contribute to the degradative process, but the exact mechanism and natural history of this chemical degradative process is

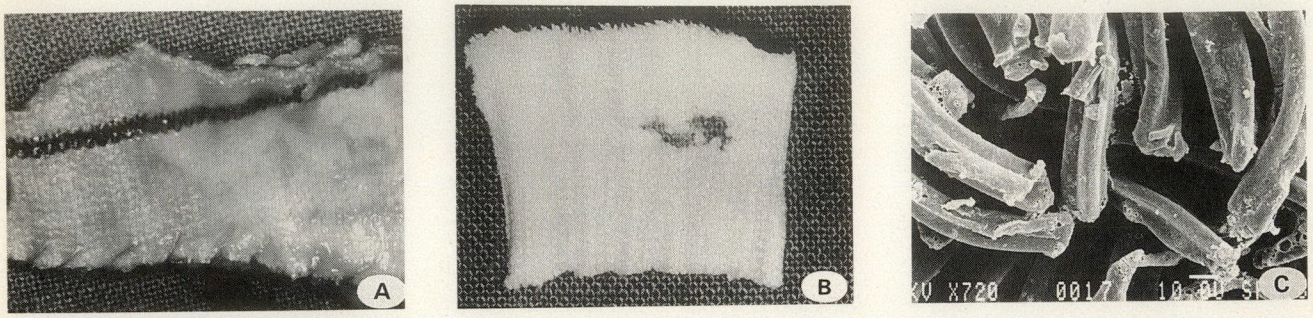

FIG. 3. (A) Marked lipid deposition in portion of graft removed from 73-year-old patient with femoral AFA that appeared 8 years after implantation. (B) Cleaned graft specimen showing area of fibre degradation at site separate from anastomosis. (C) Scanning electron micrograph demonstrating both fraying and rounded ends of trilobar fibres, reflecting chronic degradative process (original magnification × 720).

FIG. 4. (A) Cleaned graft specimen from 58-year-old patient who required reoperation for aortic AFA 6 years and 4 months after implantation. Note frayed edges on right and adjacent graft tear just proximal to bifurcation. (B) Scanning electron micrograph of area of graft tear (original magnification × 20). (C) Scanning electron micrograph showing evidence of degradation at ends of fibres (original magnification × 720).

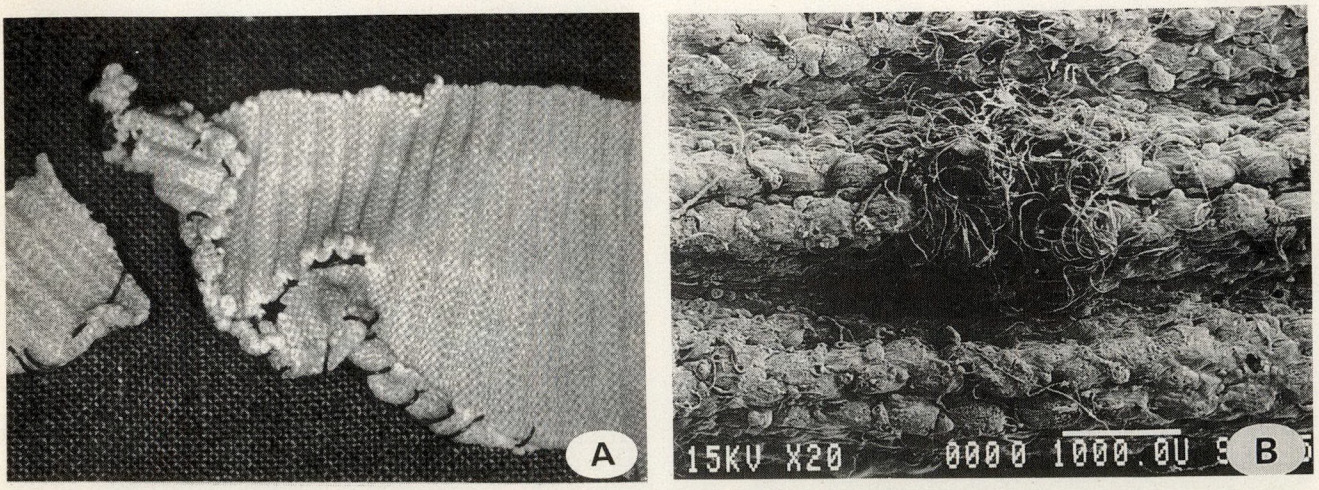

FIG. 5. (A) Cleaned graft specimen removed from 58-year-old patient who had aortobifemoral bypass performed 6 years earlier and was found to have right femoral thrombosis. Linear tear was evident just proximal to intact suture line. (B) Scanning electron micrograph demonstrating extensive residual lipid infiltration after cleansing in sodium bicarbonate baths (original magnification × 20).

not known.[4,7] Furthermore, the relative roles of lipids, bacteria and macrophages are not well defined, and further research needs to be done in this area.

The remaining group of factors related to the host artery or arterial–prosthetic junction accounted for the majority of AFAs in most recent series.[2,3,8] Compliance mismatch, stress at the anastomosis, adherence to the inguinal ligament causing traction at the anastomosis, associated hypertension or previous endarterectomy are examples of such factors and are the focus of other reports.[9–13] The most common factor reported is that of degeneration of the arterial wall, but the exact pathogenesis is not clear. The arterial wall may undergo necrosis, and subsequently fibrosis, during the healing process. This fibrosed wall gradually gives way to mechanical forces, enlarges and eventually may be detected clinically or may become symptomatic. Arterial necrosis may be secondary to suture placement combined with repeated mechanical stresses with or without overt clinical infection. Although no cases of overt infection were seen in this series, the presence of bacteria was documented by SEM in 20 of the 26 patients. Gram's staining was negative in all 18 specimens so stained, yet bacteria were seen in 15 of the specimens on SEM. This high rate of bacterial invasion is consistent with findings in the reports of Kaebnick and colleagues,[14,15] who obtained positive

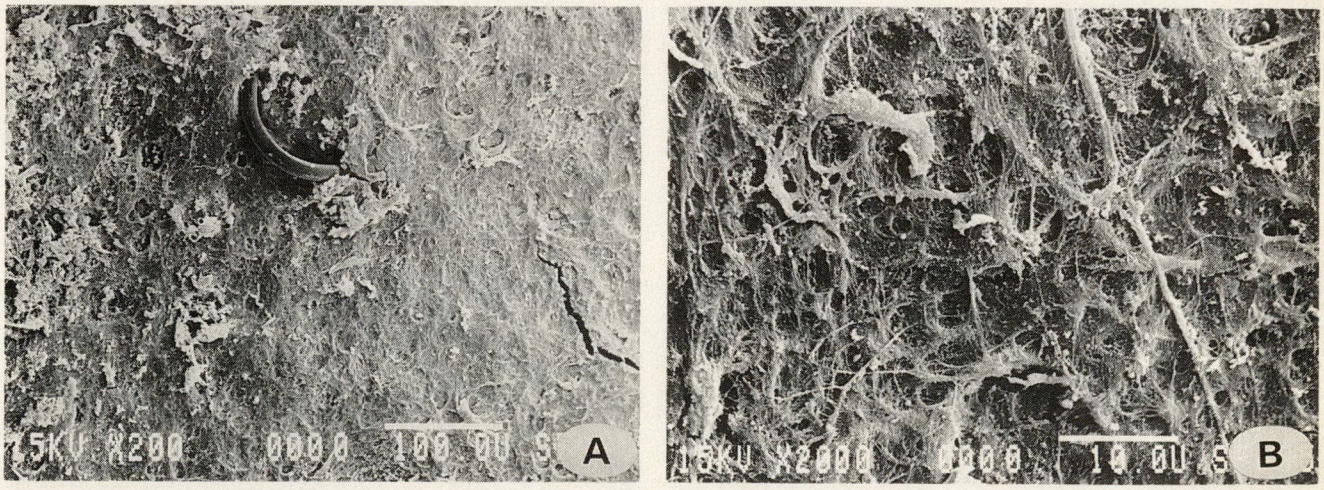

FIG. 6. Graft removed from 74-year-old patient whose aortobifemoral bypass lasted 10 years before left AFA appeared. (A) Scanning electron micrograph of internal capsule showing relatively smooth surface (original magnification × 200). (B) Note the confluence of fibrin strands at higher magnification (original magnification × 2000).

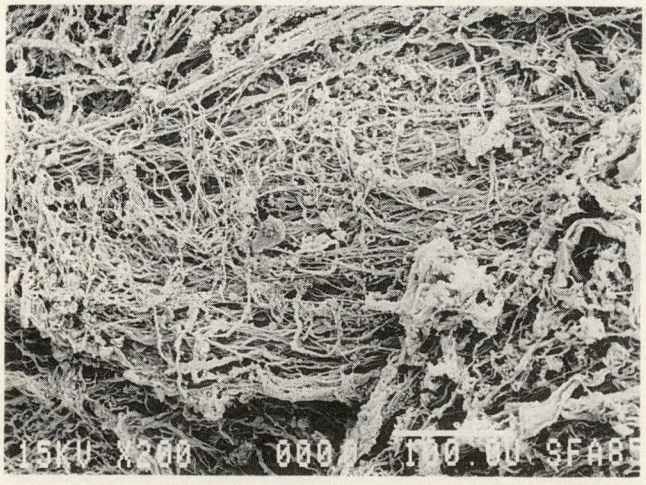

FIG. 7. Graft removed from 65-year-old patient with right femoral AFA in aortobifemoral bypass performed 6 years previously. Internal capsule shows loose fibrin strands (compare with Fig. 6B) (original magnification × 200).

FIG. 8. Scanning electron micrograph of luminal surface of graft removed from 79-year-old patient who had undergone patch iliac angioplasty for iliac stenosis 1 year earlier. Note presence of bacteria, often seen in clumps (arrows) (original magnification × 2000).

cultures in 90% of AFAs after ultrasonification of the specimens. Although samples were not taken for culture in this series and the bacteria seen by SEM cannot be typed, the most likely organism is *Staphyloccoccus epidermidis*, which may reflect contamination at the time of surgery.[16,17] The exact role of these bacteria in the pathogenesis of AFAs is unclear, and the lack of case-control grafts removed either at autopsy or for reasons other than AFA in this study makes it difficult to associate the presence of bacteria solely with AFAs. Recently, however, Martin and colleagues[18] produced anastomotic disruption in 9 (56%) of 16 dogs implanted with a graft exposed to a biofilm-producing strain of *S. epidermidis*. The additional observation of an intact and confluent internal capsule in only 3 of our 26 specimens may implicate a fibrinolytic process, which could contribute to the eventual breakdown of the fibrous wall and dehiscence of the anastomosis with formation of the AFA.

Conclusions

The etiology of AFAs is multifactorial. Factors relating to the host artery and arterial–prosthetic junction are the major ones. Bacteria were documented in 20 out of 26 specimens and may play a role in degeneration of the arterial wall leading to necrosis. Chemical fibre degradation, possibly secondary to lipid infiltration, was seen in three cases. There were no cases of suture-related failure leading to AFA formation.

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Parathyroid Cyst: Diagnosis and Treatment of an Unusual Surgical Problem

B. Mitmaker, MD, PhD, FRCSC;* S. Lerman, MD, CSPQ;† E. Lamoureux, MD, FRCPC;‡
L. Bégin, MD, FRCPC‡

A case of parathyroid cyst is reported in which the diagnosis was suggested when watery, clear fluid was aspirated from a mass found in the anterior region of the neck of a 34-year-old woman on routine medical examination. The diagnosis was confirmed by measurement of the parathormone content in the cyst fluid and by histologic examination of the cyst wall. Although rare, parathyroid cyst should be considered in the differential diagnosis of cysts in the anterior compartment of the neck.

Surgery has been the usual treatment of such cysts, but several reports have been published in which repeated aspiration resulted in the disappearance of the cyst. If conservative treatment of a parathyroid cyst is unsuccessful, the cyst should be removed surgically.

Un cas de kyste de la parathyroïde est signalé où le diagnostique a été suggéré lorsqu'un liquide aqueux, limpide a été aspiré d'une masse découverte à la région antérieure du cou d'une femme de 34 ans au cours d'un examen médical de routine. Le diagnostique a été confirmé par la mesure de la teneur en parathormone du liquide du kyste et à l'examen histologique de la paroi du kyste. Bien que rares, les kystes de la parathyroïde devraient être considérés dans le diagnostique différentiel des kystes du compartiment antérieur du cou.

La chirurgie a été utilisée comme traitement habituel de ces kystes, mais plusieurs rapports ont été publiés où l'aspiration répétée a provoqué la disparution du kyste. Si le traitement conservateur du kyste de la parathyroïde échoue, le kyste devrait être excisé.

Although microscopic cysts are common in both normal and abnormal parathyroid glands, a single parathyroid cyst, large enough to assume clinical and surgical importance, is rare.[1-4] Since the initial case report by Goris in 1905,[5] 162 such cases have been published. Despite this, the condition is hardly mentioned in modern surgical textbooks and is rarely considered in the differential diagnosis of anterior neck masses. However, awareness of this condition is worthwhile, since fine-needle aspiration of cystic masses in the neck permits the preoperative diagnosis of these lesions by determining the parathyroid hormone (PTH) levels of the cyst fluid.[6-8]

In this paper we describe a case that illustrates the value of PTH determination on the fluid aspirate of an anterior neck mass.

Case Report

An anterior neck mass was discovered during routine medical examination of a 34-year-old woman. There were no symptoms of thyroid dysfunction or local compression. There was no history of nephrolithiasis, pancreatitis or peptic ulcer disease. The family history was negative for disorders of the thyroid gland and for calcium homeostasis.

Physical examination revealed a 2 × 3-cm nodule in the region of the left lobe of the thyroid gland. The nodule was soft, mobile and nontender, and there was no regional lymphadenopathy. The clinical impression was consistent with a thyroid nodule. The initial results of tests of thyroid function were normal. Thyroid scanning with iodine-131 revealed a hypofunctioning nodule, measuring 2 × 2 cm, in the lower pole of the left lobe of the thyroid, and ultrasonography demonstrated a 4.3 × 5-cm cystic structure in the anterior compartment of the neck (Fig. 1). Fine-needle aspi-

*From the *Department of Surgery, †Department of Medicine and ‡Department of Pathology, Sir Mortimer B. Davis-Jewish General Hospital, McGill University, Montreal*

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Reprint requests to: Dr. B. Mitmaker, Department of Surgery, Sir Mortimer B. Davis-Jewish General Hospital, 3755 Côte Ste. Catherine Rd., Montreal, PQ H3T 1E2

ration biopsy yielded 10 mL of clear watery fluid and resulted in complete disappearance of the mass.

Despite repeated fine-needle aspirations the cyst recurred. Each recurrence was heralded by pain and discomfort on the left side of the neck. The watery, clear appearance of the fluid at the first aspiration had prompted the treating physician (S.L.) to measure the PTH content of the cyst fluid (Table I). The patient's serum calcium and PTH levels measured at the time of the first recurrence were normal. After the fifth recurrence of the cyst surgical exploration of the neck was carried out.

A cystic mass, 5 cm in diameter, was found. It bulged anteriorly after separation of the strap muscles overlying the left lobe of the thyroid gland. The cyst was tense and had a translucent opaque wall (Fig. 2). Dissection of the cyst from the inferior aspect of the atrophic left thyroid lobe was impossible. Consequently the entire cyst, including its attached thyroid lobe and isthmus, was excised. The parathyroid glands on the contralateral side were essentially normal. The remaining fourth parathyroid gland on the side of the cyst was not located and was assumed to be present in the resected specimen. The patient had a smooth recovery and was able to leave the hospital on postoperative day 4.

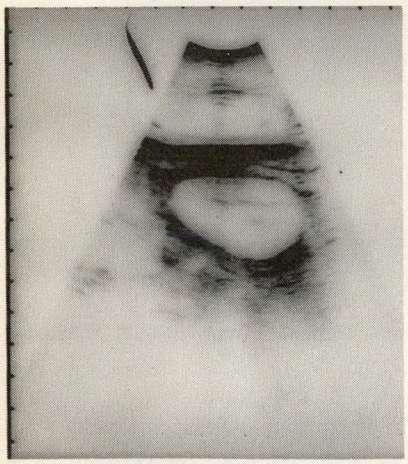

FIG. 1. Ultrasonogram shows cystic mass in left lobe of thyroid gland.

Gross examination of the specimen revealed a cyst 5 cm in diameter, attached to an atrophic left thyroid lobe. Aspiration of the cyst yielded 5 mL of clear fluid. The concentration of PTH in the aspirate was 10 000 ng/L.

Microscopic examination of multiple sections of the cyst wall revealed a fibrous shell in which was embedded in normally appearing parathyroid tissue as well as some thymic rests. The cyst wall was lined by a continuous, single layer of cuboidal wasserhelle and chief cells, each with a prominent, dense nucleus. The adjacent thyroid tissue was histologically normal. The lining epithelium of the cyst wall showed a strong cytoplasmic reaction for PTH, using an immunoperoxidase technique for this antigen (Dakopatts Corp., Mississauga, Ont.).

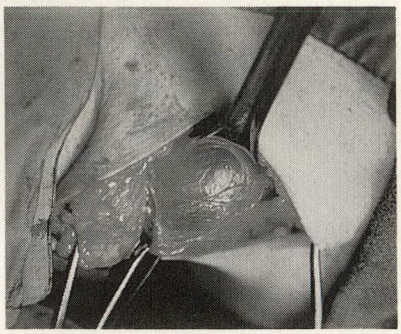

FIG. 2. Operative appearance of parathyroid cyst occupying left lobe of thyroid gland. Note translucent appearance of cyst wall.

Discussion

The presence of a clear, colourless fluid obtained from an anterior neck cyst should suggest the diagnosis of a parathyroid cyst. The performance of a PTH assay on the cyst fluid not only has enhanced the accuracy of the preoperative diagnosis, but also has influenced the treatment of 678 of these rare cases. The PTH levels of the cyst fluid reported in the literature[7,9,10] were generally extremely elevated, as in the present case. Although the majority of these clinically palpable parathyroid cysts are nonfunctional, a small number have been associated with hyperparathyroidism.[11,12] Pathologic changes in the walls of these cysts or adenomas, such as hemorrhage or necrosis, are be-

Table I. Results of Measurements Made on Aspirate of Parathyroid Cyst and Serum Measurements of Parathyroid Hormone (PTH) and Calcium

Date of recurrence	Aspirate					Serum PTH, ng/L*	Total serum calcium, mmol/L†
	Volume, mL	Colour	Cellularity	Complete disappearance	PTH, ng/L		
Oct. 1987	10	WC	Acellular	Yes	>27 000	—	—
May 1988	8	WC	Acellular	Yes	> 2 500	186	2.32
July 1988	7	WC	Acellular	Yes	> 2 500	—	—
Oct. 1988	7	WC	Acellular	Yes	> 2 500	—	—
Dec. 1988	5	WC	Acellular	No	—	—	—
Mar. 1989	10	WC	—	Yes	> 2 500	—	—

WC = water clear.
*Normal < 315 ng/mL.
†Normal 2.20 to 2.52 mmol/L.

lieved to be responsible for the hyperparathyroid crisis reported in some cases.[2,13,14]

The pathogenesis of parathyroid microcysts is uncertain. Several hypotheses have been advanced. The most common explanation for the formation of microscopic cysts ostensibly arising in normal parathyroid glands is that they result from degeneration or hemorrhage.[13,15] Other hypotheses include the retention of parathyroid secretions within colloid vesicles, developmental anomalies and the persistence of Kursteiner canals, normally found in fetal parathyroid glands.[16]

Ultimately the coalescence of these microcysts or the progressive enlargement of a single microcyst is believed to give rise to a macroscopic cyst. Others[17,18] have suggested that parathyroid cysts may be the result of infarction of parathyroid adenomas.

Clinically these rare lesions occur most commonly in the fourth and fifth decades of life. The female to male ratio is 2.5:1. Less than 10% of the cysts are associated with hyperparathyroidism. For unknown reasons, functioning parathyroid cysts are 1.6 times more common in men.[1,11,12,14,19] Most commonly the inferior parathyroid glands are involved, predominantly on the left side, as in this case. The mass is generally related to the inferior poles of the thyroid gland with most patients complaining of mild discomfort and pain in the cervical region. A cystic mass in the lower neck palpable on physical examination is usually considered to be thyroidal or branchial in origin.[2,3,8,20,21] Given the ease of fine-needle aspiration of these lesions for diagnostic purposes, the presence of a clear watery fluid should suggest this diagnosis, which can be verified by PTH assay.[6,7,9,10]

At present the initial treatment of these large parathyroid cysts is needle aspiration, since some have been known to disappear completely.[2,9,10] No reports in the literature have described the use of sclerotherapy, a method frequently used in the treatment of large thyroid cysts. Those parathyroid cysts that tend to recur after repeated aspirations are treated definitively by surgical removal.

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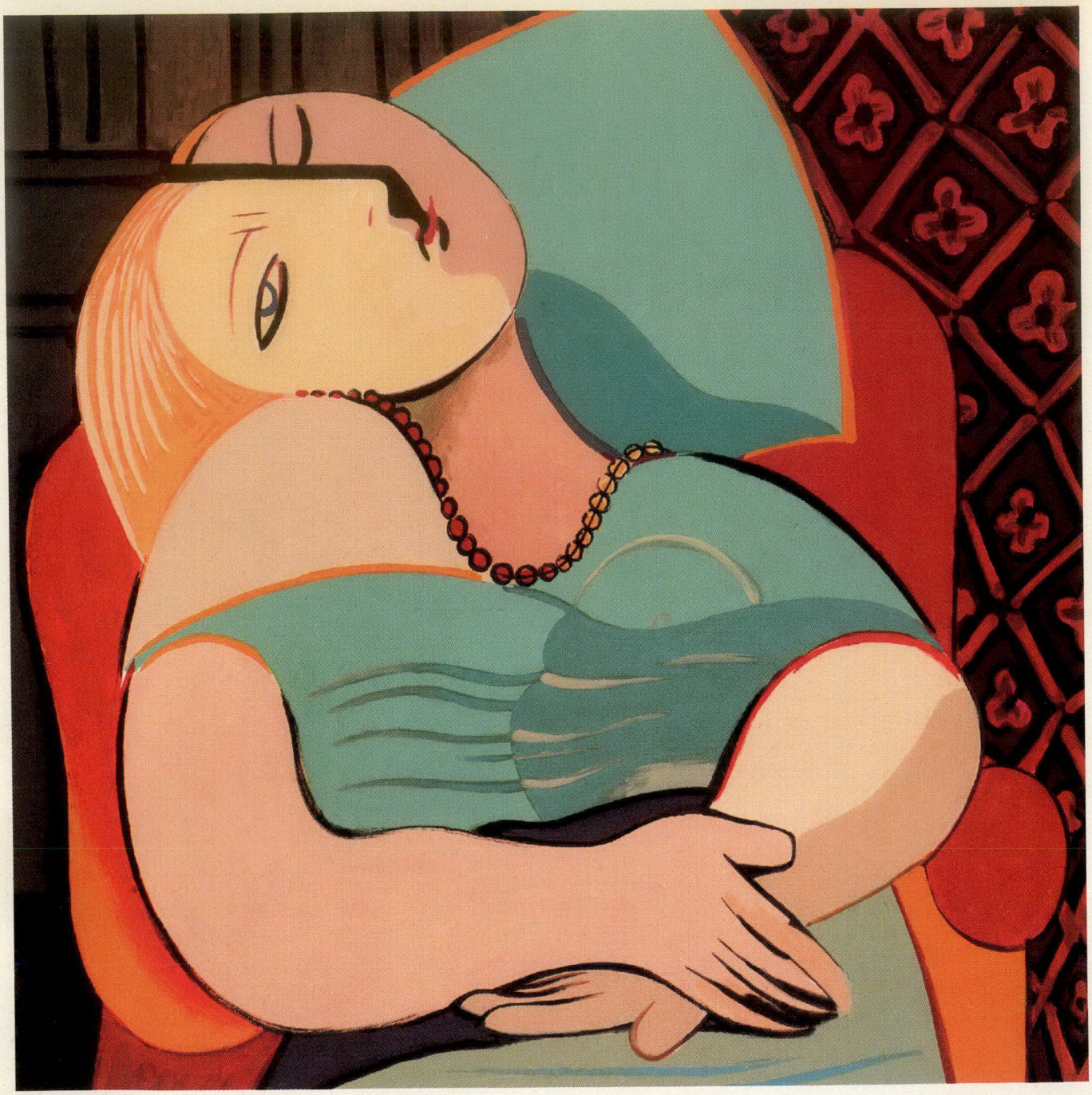

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Spinal Injuries in Ice Hockey Players, 1966-1987

Charles H. Tator, MD, PhD, FRCSC; Virginia E. Edmonds, RN, BA; Lillian Lapczak, BSc; Ira B. Tator, BA, MSc

A registry, established by the Committee on Prevention of Spinal Cord Injuries Due to Hockey, of major injuries to the spine or spinal cord sustained while playing ice hockey contains 117 cases entered between January 1966 and March 1987; 112 of these injuries were sustained in Canada. Between 1981 and 1986 up to 15 hockey related major spinal injuries were reported in Canada each year. Most injuries occurred in teenagers and players under 30 years of age who were playing in supervised games. The most common cause of injury was a push or check from behind, which caused the player to be catapulted head first into the boards.

The authors describe the programs currently being implemented to prevent the occurrence of major spinal injuries. Unfortunately, these programs have not decreased the number of injuries reported annually.

Un registre des blessures sérieuses de la moelle épinière subies par les joueurs de hockey sur glace a été établi par le Comité pour la prévention des blessures de la moelle épinière dues au hockey. Celui-ci renferme maintenent 117 cas répertoriés entre janvier 1966 et mars 1987; 112 de ces blessures ont été subies au Canada. De 1981 à 1986, jusqu'à 15 blessures sérieuses de la moelle ont été associées au hockey, chaque année, au Canada. La plupart des lésions sont survenues chez des adolescents ou chez des joueurs de moins de 30 ans qui évoluaient dans des circuits organisés. La cause de blessures la plus fréquente était une poussée ou un échec venant de l'arrière qui avait pour effet de catapulter le joueur, tête première, dans la bande.

Les auteurs décrivent les programmes actuellement mis en vigueur pour prévenir les blessures sérieuses de la moelle épinière. Malheureusement, ces programmes n'ont pas fait diminuer le nombre de lésions signalées annuellement.

Around the world, participation in sports and recreational activities has resulted in acute injury to the spinal cord,[1] although the types of activities leading to these catastrophic injuries differ between countries. In Canada diving has always been the leading cause of spinal-cord injury in the sports-recreation category;[2-4] until recently such injuries were rarely related to hockey. In a review of 55 patients who sustained acute spinal-cord injuries while participating in sports or recreational activities and were treated in two Toronto hospitals between 1948 and 1973, not a single case was hockey related.[2] The first report of spinal-cord injury associated with hockey in the Canadian literature was published in 1984.[5] No spinal-cord injuries were mentioned in reports of hockey related injuries in the English literature before 1984,[6-11] although Feriencik[7] in 1979 reported hockey related injuries to the lumbar spine in Czechoslovakia.

In 1981 the Committee on Prevention of Spinal Cord Injuries Due to Hockey was formed. Since then it has conducted research into the causes of these injuries and has developed preventive programs. The committee conducted its first Canadian national survey in 1982 to document the extent of the problem; since then, two additional surveys have been done. By March 1987, 117 hockey related spinal injuries had been reported to the registry. It should be noted that the registry is strongly supported by the Canadian Amateur Hockey Association and the Canadian Paraplegic Association.

This article provides demographic details of these 117 injuries, discusses the possible causal mechanisms and outlines the preventive

From the Canadian Sports Spine and Head Injuries Research Centre and the Division of Neurosurgery, Toronto Western Hospital, University of Toronto, Toronto

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Reprint requests to: Dr. C.H. Tator, Toronto Western Hospital, Rm. 2-003 Edith Cavell Wing, 399 Bathurst St., Toronto, ON M5T 2S8

programs introduced by the Canadian Sports Spine and Head Injuries Research Centre to reduce the incidence of these tragic injuries. It is the committee's belief that collecting data on spinal injuries in hockey is an essential part of the effort to eliminate these injuries.

Methods

The Committee on Prevention of Spinal Cord Injuries Due to Hockey conducted national surveys in 1982, 1984 and 1986. Questionnaires, in English and French, were sent to approximately 1000 neurosurgeons, orthopedic surgeons and physical medicine and rehabilitation specialists practising in Canada, asking them to report all major spinal injuries seen in their practices. Information was collected on all patients with hockey related major injuries to the spine, with or without injuries to the nerve roots or spinal cord. Excluded were minor spinal injuries such as sprains, strains, flexion–extension injuries and whiplash. In addition, case reports published in the media were collected to augment the cases reported by the physicians, although virtually every case was eventually reported by a physician. In approximately half of the cases, the information provided by the physician was augmented by information from the players, coaches and league officials. The data on the six cases occurring in the United States were submitted by physicians in the United States who became aware of the work of the committee.

For the purpose of this report, the data from the first 42 cases reported in 1984[12] have been added to the more recent cases. Thus, the present report spans the period from 1966, when the first reported case occurred, to March 1987, the date of occurrence of the last case included in this report. The data were accumulated at the Canadian Sports Spine and Head Injuries Research Centre, Toronto Western Hospital, University of Toronto, which is the research facility of the Committee on Prevention of Spinal and Head Injuries Due to Hockey. The March 1987 cut-off date was based on a report made at that time to the Canadian Amateur Hockey Association, one of the sponsors of the registry.

Results

Geographic Location

Except for the six injuries that occurred in the United States and were reported by US physicians, all injuries reported to the Committee occurred in Canada (Table I). Fifty-seven (49%) injuries occurred in Ontario; only 12 injuries (10%) occurred in Quebec. The rest of the Canadian cases were distributed across the country in proportion to the population.

Annual Incidence

The injuries occurred rarely in the 1960s and 1970s (Table II). Beginning in 1980, the number of major spinal injuries occurring annually increased markedly, and between 1982 and 1986 they numbered approximately 15/yr.

Table I. Geographic Location of Hockey Related Spinal Injuries Sustained by 117 Patients Between January 1966 and March 1987

Location	Frequency, no. (%)
Ontario	57 (49)
Quebec	12 (10)
Alberta	9 (8)
British Columbia	9 (8)
Nova Scotia	5 (4)
Saskatchewan	5 (4)
Manitoba	4 (3)
Prince Edward Island	3 (3)
Yukon Territories	3 (3)
Newfoundland	2 (2)
New Brunswick	1 (0.5)
United States	6 (5)
Unknown	1 (0.5)

Sex and Age

Of the 117 injuries, 112 (96%) occurred in boys and men and 5 (4%) occurred in girls and women. Sixty-four percent of the players were between 11 and 20 years of age, and only 19% were between 21 and 30 years of age (Table III). The youngest player to sustain a major spinal injury was 11 years old and the oldest 47 years (median 18 years, mean 21 years).

Level of Injury

Almost 80% of the injuries in-

Table II. The Number of Spinal Injuries Occurring Annually,* Reported to the Committee on Prevention of Spinal and Head Injuries Due to Hockey, From January 1966 to March 1987†

Year	Number of injuries
1966	1
1975	1
1976	2
1977	2
1978	4
1979	2
1980	8
1981	12
1982	15
1983	15
1984	15
1985	12
1986	15
1987 (to March)	6

*The injuries are recorded for the year in which they occurred rather than the year when they were reported to the committee.
†Data are missing for seven injuries.

Table III. Age of Injured Players*

Age, yr†	Frequency, no. (%)
11 – 20	75 (64)
21 – 30	22 (19)
31 – 40	7 (6)
41 – 50	3 (3)

*Data are missing for 10 cases (8%).
†Age range 11 to 47 yr, mean 21 yr, median 18 yr.

volved the cervical spine (Table IV); approximately 48% of the injuries affected C4–5, C5 and C5–6. Thoracic, thoracolumbar and lumbosacral injuries were relatively rare. The most common site of injury (15.6%) was C5–6.

Neurologic Deficit

As noted above, the registry excluded minor injuries such as vertebral strains, although fractures or dislocations of the spine were included even if they did not cause neurologic injuries. The spinal cord was affected in 52.1% of the injuries, and damage to one or more nerve roots occurred in 10.3% of the injuries (Table V). Of those whose spinal cord was injured, 29 patients sustained complete permanent spinal-cord injuries with no preservation of motor or sensory function below the level of injury, which was cervical in all cases. Of the 117 injured players, 5 were known to have died as a result of their injuries at the time of preparing this report. Most deaths were attributed to respiratory failure.

Type of Athletic Event

The largest number of injuries occurred in supervised, scheduled games within an organized hockey league (Table VI): 85 players (73%) were known to have sustained their injuries in organized games. Only a small number of injuries occurred during practices or unstructured or unsupervised events (shinny).

Mechanism of Injury

Axial loading was found to be the most common mechanism causing cervical-spine and cervical-cord injury. Axial loading was applied to the head when the helmeted head struck another object, especially the boards. The event that precipitated the injury was usually a push or check from behind (31 injuries, 26.5%). In most instances the player was completely unsuspecting of the impact and was hurled horizontally into the boards; the cervical spine was crushed between the abruptly halted, helmeted head and the torso. In most instances the axial loading was applied with the head in neutral alignment with the neck and torso or in slight flexion. Major degrees of flexion or extension were much less common. Impact with the boards accounted for 76 injuries (65%) (Table VII). Impact between players was the cause of injury in 10.3%; injuries caused by impact with the ice (2.6%) or goal post (0.9%) occurred less frequently. In most cases the player collided with the boards (Table VIII). Other frequent causes of injury were pushes and checks from the front and from the sides, especially into the boards. In many of these injuries, impact with the boards produced the spinal injury.

Table IV. Vertebral Level of Spinal Injury*

Vertebral level	Frequency, no. (%)
Cervical, C1 – C7, T1	93 (79.5)
Thoracic, T1 – T11	3 (9.2)
Thoracolumbar, T11/12 – L1/2	7 (6.0)
Lumbosacral, L2 – S5	6 (5.1)

*Data are missing for 8 cases (6.8%).

Table V. Neurologic Type of Injury ($n = 73$)*

Type of injury	Frequency, no. (%)
Spinal cord injury	
Complete motor and complete sensory loss	29 (24.8)
Complete motor and incomplete sensory loss	9 (7.7)
Incomplete motor loss and incomplete sensory loss	21 (17.9)
Incomplete sensory loss	2 (1.7)
Root injury only	12 (10.3)

*No neurologic injury in 28 cases (23.9%). Data were missing or incomplete in 16 cases (13.7%).

Table VI. Type of Hockey Played When Spinal Injury Occurred*

Type of play	Frequency, no. (%)
Organized games	85 (73)
Practices	4 (3)
Unstructured play (shinny)	1 (1)
Unknown	27 (23)

Table VII. Type of Collision*

Type of collision	Frequency, no. (%)
Boards	70 (59.8)
Other players	12 (10.3)
Ice	3 (2.6)
Goal post	1 (0.9)
Boards and players†	5 (4.3)
Players and ice†	1 (0.9)
Players and goal post†	1 (0.9)
Boards and ice†	1 (0.9)

*Data were incomplete or missing in 23 cases (19.7%).
†More than one type of collision.

Table VIII. Mode of Injury*

Mode of injury	Frequency, no. (%)
Single mechanisms	
Pushed or checked from behind	26 (22.2)
Pushed or checked	15 (12.8)
Slide	6 (5.1)
Tripped on ice	10 (8.5)
Trip or fall	3 (2.6)
Tripped by player	3 (2.6)
Slide with player	1 (0.9)
Lost balance	2 (1.7)
Missed check	2 (1.7)
Multiple mechanisms	
Tripped on ice + slide	3 (2.6)
Tripped on ice + slide with player	1 (0.9)
Trip + fall	1 (0.9)
Slide + pushed or checked	2 (1.7)
Slide + pushed or checked from behind	5 (4.3)
Trip or fall + pushed or checked	1 (0.9)
Slide + tripped by player	1 (0.9)

*Data incomplete or missing in 35 cases (29.9%).

Other Features

Burst fractures and fracture–dislocations were the most frequent types of vertebral injuries. There was one case of a ruptured cervical disc that caused an incomplete spinal-cord injury. Cases were reported of hockey players who had cervical-spine stenosis with neurapraxia and transient traumatic quadriparesis, which was described in football players by Torg, Pavlov and Genuario.[13,14] However, spinal stenosis in hockey players was not accurately documented in this study.

Almost all the players in this series were wearing helmets, and more than two-thirds were wearing face masks. Only three cases of serious hockey related head injury were reported to the Committee between 1981 and 1987.

Discussion

Unfortunately, hockey related spinal-cord injuries have not declined during the interval since 1984 when we reported the results of the first national survey. From 1966 to March 1987, we recorded 117 cases of hockey related spinal injury, including five deaths. The Committee received reports of 12 to 15 such injuries occurring each year in Canada between 1981 and 1986. In 1985 the Canadian Amateur Hockey Association instituted a rule prohibiting pushing or checking from behind. Either the rule has not been enforced as vigorously as it should be, or the time required for the referees, coaches and players to adjust their behaviour has not been sufficient. A push or check, causing the top of the helmeted head to strike the boards was the most common mechanism. Young men in their teens and early 20s playing organized hockey were at greatest risk of spinal injury; nearly three-quarters of the injuries occurred during organized games. Only 4% of the known cases involved injuries incurred during practice or shinny. This finding is fundamental in terms of injury prevention. It also is reflected in some of the recent American literature. For example, Gerberich and colleagues[15] also found that the majority of injuries occurred during organized games, and in their study from Minnesota,[15] 82.3% of all hockey injuries occurred during games.

Efforts to prevent spinal-cord injury in hockey must address the rudimentary problem of aggression during the game. In the Minnesota study, players were asked to rank their reasons for playing the game. Extraordinarily, those players who noted in their first or second ranking that playing hockey was a means of ridding tension and aggression ran a fourfold risk of concussion.[15] Recognition of this attitude may be important in isolating the causes and developing preventive strategies.

As in the initial analysis of the first 42 cases,[12] there was a sharp contrast between the numbers of reported cases from Quebec and Ontario — 10% versus 49% (Table I). Although Ontario has more hockey players than Quebec, the number of injuries exceeds an explanation on this basis. Indeed, the authors believe that differences in organization and player attitude may account for this major disparity. The correlation between methods of coaching and refereeing and the incidence of injuries needs to be carefully scrutinized.

From an epidemiologic viewpoint it is worthwhile to review some of the conclusions drawn from the literature on American football. Although the incidence of head injuries was markedly reduced during the 1960s and 1970s due to the use of helmets, the incidence of spinal-cord injuries may have increased,[16] according to the results of excellent epidemiologic studies of injuries documented by two athletic injury reporting systems.[16,17] It was concluded that the helmeted head was being used as an offensive weapon to spear the opponent. Head-first tackling and blocking were disallowed, and since then there has been a marked reduction in the incidence of spinal-cord injuries in football.[18] In the late 1970s and early 1980s, the annual number of cases of quadriplegia in football players decreased from about 30 to 10.[17] There are approximately four cases of quadriplegia a year in Canada due to hockey. Thus, on a per capita basis, hockey in Canada causes approximately three times as many cases of quadriplegia annually as does football in the United States. In terms of the risk of spinal-cord injury, participation in hockey appears to be much riskier than participation in football, especially in Ontario, although we have not been able to obtain exact data on the numbers of participants.

Analysis of Etiologic Factors

Hockey related spinal injury is a recent phenomenon; the Canadian Sports Spine and Head Injuries Research Centre has identified several causal factors. In our opinion, no single factor is responsible for these tragic accidents, but rather the origin is multifactorial.

It should be noted that hockey has also been associated with a high incidence of non-spinal injuries. For example, a survey in 1986 found that hockey caused the highest number of major injuries of all types in sports or recreational activities in the Province of Ontario. Indeed, 79 of the 530 major injuries sustained while participating in all types of sports and recreational

activities during 1986 were hockey related; the next most frequent causes of injury were water and motor sports.[19]

Head injuries, including face, scalp and brain injuries comprised 40% to 50% of all injuries in ice hockey before the introduction of helmets and face masks.[20-23] But, even with the use of helmets, head injuries still constitute about one-quarter of hockey injuries.[24] Most of the remaining injuries are to the limbs, especially the lower limbs.[25]

The following factors appear to be significant to the current high incidence of spinal-cord injuries in ice hockey:

- *Physical factors related to current players.* Hockey players are now taller and heavier and skate faster than players in former years. The increased weight and speed raise the forces generated by collisions.
- *Social and psychologic factors among young hockey players.* There is an increased willingness to take risks as youthful players try to emulate the violence and aggression of professional players. Unfortunately, most of these young players have neither the physical fitness nor the conditioning of professionals. There is a feeling of invincibility among young players, most likely related to the large amount of protective equipment worn. Indeed, many of the victims interviewed were completely unaware of the possibility of spinal injury in hockey.
- *Rules and refereeing.* Frequently the rules were not enforced. Many of the victims were injured during illegal play, especially pushing or checking from behind.
- *Coaching.* There was insufficient emphasis on physical conditioning, especially of the neck muscles. The players did not receive sufficient instruction about the risks of hockey and the methods of protecting the spine from injury. Some coaches overemphasized body contact and underemphasized protective manoeuvres, especially avoiding impact with the boards and strategies for impacting safely. The marked disparity in the incidence of these injuries between Ontario and Quebec suggests that attitude and coaching techniques were extremely important etiologic factors. It is of major importance that there have been no recent reports of hockey related spinal injuries from Europe, where hockey is played extensively in several northern countries.
- *Hockey rinks and equipment.* Small rinks have been considered a possible factor because collisions may be more frequent in smaller rinks. The lack of shock absorption of the boards in most rinks has been questioned as a possible etiologic factor. The use of helmets became widespread in Canadian hockey in the 1970s and preceded by several years the marked increase in neck injuries. However, biomechanical studies have not supported the notion that the helmet is an important factor.[26] It should be noted that helmets have been extremely effective in reducing the incidence of brain injuries in hockey players. Before the widespread use of helmets approved by the Canadian Standards Association, fatal brain injuries were not uncommon in hockey.[27,28] We registered only three cases of severe brain injury between 1981 and 1987. Nevertheless, we would encourage further research into helmet design. Sim and Simonet[25] have recently commented with respect to head and neck injuries in hockey that "Helmet design has been improved, but few researchers have specifically studied how well newer helmets absorb impact and prevent injury."

We do not know if poorly fitting helmets contributed to any of the injuries in this series, but we do not believe this was a significant factor. There is little evidence that a neck protector such as a roll-type collar will prevent any of these injuries and will not substitute for the extensive neck conditioning exercises we have called for. Face masks have produced a remarkable reduction of eye and dental injuries in hockey.[29,30] We found no evidence that face masks are related to the increase in spinal-cord injuries, as has been suggested.[31]

Prevention Programs

The Committee on Prevention of Spinal and Head Injuries Due to Hockey has developed several specific preventive programs to reduce the incidence of these tragic spinal injuries.

Player education and conditioning. Canadian hockey leagues and organizations have accepted the responsibility for reducing the incidence of these injuries by improving player awareness and coaching techniques, and by changing and enforcing rules. Players are being made aware of the risks of certain aspects of play, especially going into the boards face first and "blindly." Several defensive tactics for avoiding spinal injuries are being taught, especially avoiding impact of the helmeted head with the boards, the ice surface or other players. A videotape entitled "Smart Hockey" was produced in 1988 by the Committee, and is being distributed widely to leagues and schools. Coaches and league officials are encouraging players to perform specific exercises to strengthen the neck muscles; these are detailed in a brochure *Neck and Spine Conditioning for Hockey Players,* which has been distributed to all hockey players since 1984 and is also included with the videotape.

Rules and refereeing. The hockey leagues have taken a leading role in encouraging positive attitudes toward injury reduction and safe hockey. In 1985 the Canadian Amateur Hockey Association introduced specific rules against pushing or checking from behind, and the association has resolved to reduce violence in the game by enforcing the rules.

Equipment manufacturers and rink contractors. Further research is required to improve the safety of hockey equipment. Although some excellent research has been done,[26,32] further research on helmets must be done on shape, friction and shock absorption. Research into the shock absorption of the boards should be conducted. Placement of unyielding backing, such as concrete blocks, behind the boards should be discouraged. The leagues have adopted other safety measures, including the use of magnetic goalposts, and are promoting increasing the size of rinks to international standards. Perhaps low-interest federal or provincial loans could be made available to ease the burden of changing to the larger, European-size rinks.

Sports medicine experts. Specialists in sports medicine and other recreation researchers should be encouraged to continue research into spinal injuries. It is essential to continue an organized reporting system to assess the effectiveness of the preventive programs.[33] Further epidemiologic and biomechanical research should be strongly encouraged and supported by the hockey associations and by provincial, state and federal governments.

We hope that hockey will follow the excellent example set by the US football program, which reduced the incidence of major spinal-cord injuries by improving awareness and attitude and by effecting rule changes.[16-18,34]

Summary

Major spinal injuries have been recognized as a common problem in Canadian ice hockey only during the 1980s. The causes of these injuries have been found to be multifactorial. The increased weight, height, speed and aggressiveness of hockey players are important factors. Lack of awareness of the hazards of small rinks and of certain high-risk manoeuvres such as checking or pushing from behind are also important factors. Until 1985 there were no specific rules against checking or pushing from behind. Lack of neck-muscle strengthening and the player's feeling of invincibility when outfitted in modern equipment have set the stage for these tragic injuries. After these factors were identified, specific measures were taken to correct them, and a reporting system was established in Canada so that the effects of the preventive programs could be monitored. Greater awareness of the risk factors by players, coaches, leagues officials, referees and parents promises to be an effective prophylactic measure. The current, specific preventive programs involve the hockey associations, players, equipment manufacturers, health care professionals, researchers and governments.

The Canadian Sports Spine and Head Injuries Research Centre is grateful to the Ontario Ministry of Tourism and Recreation, the Canadian Amateur Hockey Association, the National Hockey League Players Association, the Canadian Paraplegic Association, Mr. Jack Cooper and Cooper Canada for funds to carry on this research. The technical assistance of Maria Vespa and Bev Woods is gratefully acknowledged.

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SESAP VI Critique

Item 145

The incidence of pneumococcal sepsis is higher among patients who have had splenectomy than in the general population. Patients with otherwise normal reticuloendothelial systems are largely able to compensate for the loss of their spleen. In otherwise normal patients, the incidence of overwhelming sepsis after splenectomy varies in several large series from approximately 1.5% (with a 50% mortality) to 3% (with a 30% mortality). Thus, the risk of dying from overwhelming sepsis in otherwise normal patients after splenectomy approximates 1%. The probability of sepsis rises significantly (to 20% to 30%) in patients with certain hematologic diseases such as thalassemia and other abnormalities of the reticuloendothelial system. Polyvalent pneumococcal vaccines can reduce this risk somewhat. Because these vaccines do not protect against all serotypes of pneumococci, however, and because sepsis can be produced by other organisms, the protection is approximately 30%.

B

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PRIMAXIN®

(imipenem and cilastatin sodium for injection)

Antibiotic

CNS adverse experiences such as myoclonic activity, confusional states, or seizures have been reported with PRIMAXIN® especially when recommended dosages based on renal function and body weight were exceeded. These experiences have occurred most commonly in patients with CNS disorders (e.g., brain lesions or history of seizures) and/or who have compromised renal function. However, there were rare reports in which there was no recognized or documented underlying CNS disorder. Close adherence to recommended dosage schedules is urged, especially in patients with known factors that predispose to seizures.

ACTION

Imipenem exerts a bactericidal action by inhibiting cell wall synthesis in aerobic and anaerobic gram-positive and gram-negative bacteria.

PRIMAXIN® consists of two components: (1) imipenem, a derivative of thienamycin, a carbapenem antibiotic; and (2) cilastatin sodium, a specific inhibitor of dehydropeptidase-I a renal enzyme which metabolizes and inactivates imipenem. Cilastatin blocks the metabolism of imipenem in the kidney, so that concomitant administration of imipenem and cilastatin allows antibacterial levels of imipenem to be attained in the urine.

Inhibition of cell-wall synthesis is achieved in gram-negative bacteria by the binding of imipenem to penicillin binding proteins (PBPs). In the case of *Escherichia coli* and selected strains of *Pseudomonas aeruginosa*, imipenem has been shown to have highest affinity for PBP-2, PBP-1a and PBP-1b, with lower activity against PBP-3. The preferential binding of imipenem on PBP-2 and PBP-1b leads to direct conversion of the individual cell to a spheroplast resulting in rapid lysis and cell death without filament formation. When imipenem is removed prior to complete killing of gram-negative species, the remaining viable cells show a measurable lag, termed a "post-antibiotic effect" (PAE), prior to resumption of new growth.

INDICATIONS AND CLINICAL USE

PRIMAXIN® (imipenem and cilastatin sodium for injection) may be indicated in the treatment of serious infections when caused by sensitive strains of bacteria. Where considered necessary, therapy may be initiated on the basis of clinical judgment before results of sensitivity testings are available. Continuation of therapy should be reevaluated on the basis of bacteriological findings and of the patient's clinical condition.

Imipenem is active *in vitro* against a wide range of gram-positive and gram-negative aerobic and anaerobic bacteria, including most strains which are beta-lactamase producing. Patients have responded while under treatment with PRIMAXIN® for single or mixed infections of the following body systems, when they were associated with a number of pathogenic species and strains of the genera listed:

1. Lower Respiratory Tract Infections
2. Urinary Tract Infections
3. Intra-Abdominal Infections
4. Gynecological Infections
5. Septicemia
6. Endocarditis caused by *Staphylococcus aureus*
7. Bone and Joint Infections
8. Skin Structure Infections

Gram-positive Aerobes

- *Listeria monocytogenes*
- *Nocardia asteroides*
- *Staphylococcus* (excluding many strains which are methicillin resistant)
- *Streptococcus* (excluding *S. faecium*)

Gram-negative Aerobes

- *Acinetobacter*
- *Citrobacter*
- *Enterobacter*
- *Escherichia coli*
- *Haemophilus influenzae*
- *Haemophilus parainfluenzae*
- *Klebsiella*
- *Morganella morganii*
- *Neisseria*
- *Proteus* (indole positive and indole negative strains)
- *Providencia*
- *Pseudomonas aeruginosa*
- *Serratia marcescens*

Gram-positive Anaerobes

- *Clostridium* (excluding *C. difficile*)
- *Peptococcus*
- *Peptostreptoccus*

Gram-negative Anaerobes

- *Bacteroides fragilis*
- *Bacteroides* (non-fragilis)

CONTRAINDICATIONS

PRIMAXIN® (imipenem and cilastatin sodium for injection) is contraindicated in patients who have shown hypersensitivity to either component of this product.

WARNINGS

PRIMAXIN® (imipenem and cilastatin sodium for injection) SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO STRUCTURALLY-RELATED DRUGS. IF AN ALLERGIC REACTION TO PRIMAXIN® OCCURS, DISCONTINUE THE DRUG. SERIOUS HYPERSENSITIVITY REACTIONS MAY REQUIRE EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis

Pseudomembranous colitis has been reported with the use of PRIMAXIN®. Therefore it is important to consider this diagnosis in patients who develop diarrhea during or after therapy. This colitis may range from mild to life threatening in severity.

Mild cases of pseudomembranous colitis may respond to drug discontinuance alone. In more severe cases, management may include sigmoidoscopy, appropriate bacteriological studies, fluid, electrolyte and protein supplementation, and the use of a drug such as oral vancomycin, as indicated. Other causes of colitis should also be considered.

PRECAUTIONS

General

Prolonged use of PRIMAXIN® (imipenem and cilastatin sodium for injection) may result in overgrowth of resistant organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

CNS adverse experiences such as myoclonic activity, confusional states, or seizures have been reported with PRIMAXIN® especially when recommended dosages based on renal function and body weight were exceeded. These experiences have occurred most commonly in patients with CNS disorders (e.g., brain lesions or history of seizures) and/or who have compromised renal function. However, there were rare reports in which there was no recognized or documented underlying CNS disorder. Close adherence to recommended dosage schedules is urged especially in patients with known factors that predispose to seizures (see DOSAGE AND ADMINISTRATION). Anticonvulsant therapy should be continued in patients with a known seizure disorder. If focal tremors, myoclonus, or seizures occur, patients should be evaluated neurologically and placed on anticonvulsant therapy if not already instituted. If CNS symptoms continue, the dosage of PRIMAXIN® should be decreased or discontinued.

Use in Patients with Impaired Renal Function

Dosage in patients with impaired renal function is based on the severity of infection but the maximum daily dose varies with the degree of renal functional impairment (see DOSAGE AND ADMINISTRATION - Dosage in Patients with Renal Insufficiency).

Use in Pregnancy

The use of PRIMAXIN® in pregnant women has not been studied, therefore, PRIMAXIN® should be used during pregnancy only if clearly needed. Use of this drug in women of childbearing potential requires that the anticipated benefits be weighed against possible hazards.

Reproduction studies with bolus I.V. doses suggest an apparent intolerance to PRIMAXIN® (including emesis, inappetence, body weight loss, diarrhea and death) at doses equivalent to the average human dose in pregnant rabbits and cynomolgus monkeys that is not seen in non-pregnant animals in these or other species. In other studies, PRIMAXIN® was well tolerated in equivalent or higher doses (up to 11 times the average human dose) in pregnant rats and mice (see REPRODUCTION STUDIES under TOXICOLOGY in the complete monograph).

Nursing Mothers

It is not known whether PRIMAXIN® is excreted in milk. If the use of PRIMAXIN® is deemed essential, the patient should stop nursing.

Pediatric Use

Efficacy and tolerability in infants under the age of 3 months have not yet been established; therefore, PRIMAXIN® is not recommended in the pediatric age group below the age of 3 months.

Drug Interactions

Concomitant administration of PRIMAXIN® and probenecid results in only minimal increases in plasma levels of imipenem and plasma half-life. It is not recommended that probenecid be given with PRIMAXIN®.

PRIMAXIN® should not be mixed with or physically added to other antibiotics. PRIMAXIN® has been administered concomitantly with some antibiotics, such as aminoglycosides.

There is no evidence to suggest that association of PRIMAXIN® with any other beta-lactam antibiotics has any therapeutic advantage.

ADVERSE REACTIONS

PRIMAXIN® (imipenem and cilastatin sodium for injection) is generally well tolerated. The following adverse reactions were reported on 1,723 patients treated in clinical trials. Many of these patients were severely ill and had multiple background diseases and physiological impairments, making it difficult to determine causal relationship of adverse experiences to therapy with PRIMAXIN®.

Local Adverse Reactions

Adverse local clinical reactions that were reported as possibly, probably or definitely related to therapy with PRIMAXIN® were:

	Incidence (%)
Phlebitis/thrombophlebitis	1.7
Infused vein pain	0.6
Vein induration	0.2
Infused vein infection	0.1

Systemic Adverse Reactions

Adverse clinical reactions that were reported as possibly, probably, or definitely related to PRIMAXIN® were:

	Incidence (%)
Gastrointestinal	
nausea	2.0
diarrhea	1.7
vomiting	1.6
tongue papillar hypertrophy	0.2
pseudomembranous colitis (see WARNINGS)	0.1
hemorrhagic colitis	<0.1
gastroenteritis	<0.1
abdominal pain	<0.1
glossitis	<0.1
heartburn	<0.1
pharyngeal pain	<0.1
increased salivation	<0.1
CNS	
fever	0.4
dizziness	0.3
seizures (see PRECAUTIONS)	0.2
somnolence	0.2
confusion	0.2
myoclonus	0.1
vertigo	0.1
headache	0.1
encephalopathy	<0.1
paresthesia	<0.1
Special Senses	
transient hearing loss in patients with impaired hearing	<0.1
tinnitus	<0.1
Respiratory	
dyspnea	0.1
hyperventilation	<0.1
thoracic spine pain	<0.1

Cardiovascular

hypotension	0.4
palpitations	0.1
tachycardia	<0.1

Renal

oliguria/anuria	<0.1
polyuria	<0.1

Skin

rash	0.9
pruritus	0.3
urticaria	0.2
skin texture changes	0.1
candidiasis	0.1
erythema multiforme	<0.1
facial edema	<0.1
flushing	<0.1
cyanosis	<0.1
hyperhidrosis	<0.1
pruritus vulvae	<0.1

Body as a whole

polyarthralgia	<0.1
asthenia/weakness	<0.1

Adverse Laboratory Changes

Adverse laboratory changes, without regard to drug relationship, that were reported during clinical trials were:

Hepatic: Increased SGPT, SGOT, alkaline phosphatase, bilirubin and LDH.

Hemic: Increased eosinophils, positive Coombs test, decreased WBC and neutrophils, increased WBC, increased platelets, decreased platelets, decreased hemoglobin and hematocrit, increased monocytes, abnormal prothrombin time, increased lymphocytes, increased basophils.

Electrolytes: Decreased serum sodium, increased potassium, increased chloride.

Renal: Increased BUN, creatinine.

Urinalysis: Presence of urine protein, urine red blood cells, urine white blood cells, urine casts, urine bilirubin, and urine urobilinogen.

TREATMENT OF OVERDOSAGE

There are no data available on overdosage.

PRIMAXIN® (imipenem and cilastatin sodium for injection) is cleared by hemodialysis.

DOSAGE AND ADMINISTRATION

The dosage recommendations for PRIMAXIN® (imipenem and cilastatin sodium for injection) represent the quantity of imipenem to be administered by I.V. infusion only. An equivalent amount of cilastatin is also present in the solution.

The dosage of PRIMAXIN® should be determined by the severity of the infection, renal function, body weight, the antibiotic susceptibility of the causative organism(s) and the condition of the patient. Doses cited are based on body weight of 70 kilos.

The median duration of treatment with PRIMAXIN® in clinical trials for infections of the various body systems ranged from 6 to 10 days except for endocarditis and bone and joint infections for which the median duration of treatment was 4 weeks.

Dosage in Adults

The recommended daily dose is 1 to 2 g administered in equally divided doses every 6 to 8 hours (see Table 1).

TABLE 1

ADULT DOSAGE OF PRIMAXIN®

Severity of infection	I.V. Administration Dose (mg of imipenem)	Dosage Interval	Daily Dose
Mild	250 mg	6 h	1.0 g
Moderate	500 mg	8 h	1.5 g
Severe (fully susceptible)	500 mg	6 h	2.0 g
Severe× infections due to less susceptible organisms or life threatening conditions	1000 mg 1000 mg	8 h 6 h	3.0 g 4.0 g

× Primarily some strains of *Ps. aeruginosa*.

The maximum daily dose should not exceed 4 g or 50 mg/kg, which ever is less.

Dosage in Elderly Patients

The recommended dosage of PRIMAXIN® in elderly patients with normal renal function is the same as given for adults above. Renal status of elderly patients may not be accurately portrayed by measurement of BUN or creatinine alone. Determination of creatinine clearance is suggested to provide guidance for dosing in such patients.

Dosage in Patients with Renal Insufficiency

Patients with creatinine clearances of ≤5 mL/min/1.73 m² (≤0.08 mL/s/1.73 m²) should not receive PRIMAXIN® unless hemodialysis is instituted within 48 hours. Both imipenem and cilastatin are cleared from the circulation during hemodialysis. The patient should receive PRIMAXIN® after hemodialysis and at 12 hour intervals timed from the end of that hemodialysis session. Dialysis patients, especially those with background CNS disease, should be carefully monitored; for patients on hemodialysis, PRIMAXIN® is recommended only when the benefit outweighs the potential risk of seizures (see PRECAUTIONS). Currently, there are inadequate data to recommend the use of PRIMAXIN® in patients undergoing peritoneal dialysis.

TABLE 2

MAXIMUM DOSAGE OF PRIMAXIN® IN RELATION TO RENAL FUNCTION

RENAL FUNCTION	CREATININE CLEARANCE mL/min/1.73 m² (mL/s/1.73 m²)	DOSE (g)	DOSAGE INTERVAL (h)	MAXIMUM TOTAL DAILY DOSAGE (g)
Mild impairment	31 - 70 (0.52 - 1.17)	0.5	6 - 8	1.5 - 2
Moderate impairment	21 - 30 (0.35 - 0.50)	0.5	8 - 12	1 - 1.5
Severe× impairment	0 - 20 (0 - 0.33)	0.25 - 0.5	12	0.5 - 1.0××

× Patients with creatinine clearance of 6 to 20 mL/min/1.73 m² (0.1 - 0.3 mL/s/1.73 m²) should be treated with 250 mg (or 3.5 mg/kg whichever is lower) every 12 hours for most pathogens. When the 500 mg dose is used in these patients, there may be an increased risk of seizures.

×× The highest dose is only recommended for infections due to less susceptible organisms primarily some strains of *Ps. aeruginosa*.

When only the serum creatinine level is available, the following formula (based on sex, weight, and age of the patient) may be used to convert this value into creatinine clearance (mL/min). The serum creatinine should represent a steady state of renal function.

Males: $$\frac{\text{Weight (kg)} \times (140 - \text{age})}{72 \times \text{serum creatinine (mg/100 mL)}}$$

Females: 0.85 x above value.

When using the International System of units (SI), the estimated creatinine clearance (mL/s) in males can be calculated as follows:

$$\frac{(\text{lean body weight, kg}) \times (140 - \text{age, years}) \times 1.4736}{(72) \times (\text{serum creatinine concentration, } \mu\text{mol/L})}$$

and in females the estimated creatinine clearance (mL/s) is:

$$\frac{(\text{lean body weight, kg}) \times (140 - \text{age, years}) \times 1.2526}{(72) \times (\text{serum creatinine concentration, } \mu\text{mol/L})}$$

PRIMAXIN® is cleared by hemodialysis. After each dialysis session the dosage schedule should be restarted.

Dosage in Infants and Children

The recommended total daily dosage of PRIMAXIN® in children and infants 3 months of age and older is 60 to 100 mg/kg of body weight divided into 4 equal doses given at six hour intervals. The higher dosages should be used for infants and young children. The total daily dosage should not exceed 2 grams. Clinical data are insufficient to recommend an optimum dose for infants and children with impaired renal function.

Administration

CAUTION: CONTENTS OF VIALS NOT FOR DIRECT INFUSION.

Each reconstituted 250 mg or 500 mg dose should be given by intravenous infusion over twenty to thirty minutes. Each 1000 mg dose should be infused over 40 to 60 minutes. In patients who develop nausea during the infusion, the rate of infusion may be slowed.

RECONSTITUTION

Contents of the vials must be suspended and transferred to 100 mL of an appropriate infusion solution.

A suggested procedure is to transfer approximately 10 mL from the 100 mL of the appropriate infusion solution to the vial (see list of diluents under COMPATIBILITY AND STABILITY). Shake well. Return the resulting 10 mL of suspension to the remaining 90 mL of the infusion solution.

Repeat, using 10 mL of the diluted suspension, to ensure complete transfer of the contents of the vial to the infusion solution.

CAUTION: CONTENTS OF VIALS NOT FOR DIRECT INFUSION.

COMPATIBILITY AND STABILITY

List of diluents

0.9% Sodium Chloride Injection
5% or 10% Dextrose Injection
5% Dextrose Injection with 0.02% sodium bicarbonate solution
5% Dextrose and 0.9% Sodium Chloride Injection
5% Dextrose Injection with 0.225% or 0.45% saline solution
NORMOSOL-M in D5-W
5% Dextrose Injection with 0.15% potassium chloride solution
Mannitol 2.5%, 5% and 10%

Reconstituted solutions

Solutions of PRIMAXIN® range from colourless to yellow. Variations of colour within this range do not affect the potency of the product.

PRIMAXIN®, as supplied in vials and reconstituted as above maintains satisfactory potency for four hours at room temperature and for 24 hours under refrigeration (4°C). PRIMAXIN® has been found to be stable in 0.9% Sodium Chloride Injection for 10 hours at room temperature and 48 hours under refrigeration.

DOSAGE FORMS

AVAILABILITY

PRIMAXIN® is supplied as a sterile powder mixture in vials containing imipenem anhydrous and cilastatin sodium as follows:

3514 Ca - 250 mg imipenem equivalent and 250 mg cilastatin equivalent in vials.

3516 Ca - 500 mg imipenem equivalent and 500 mg cilastatin equivalent in vials.

STORAGE

The dry powder should be stored at a temperature below 30°C.

FULL PRODUCT MONOGRAPH AVAILABLE ON REQUEST

(318-b,1,89)

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PRESCRIBING INFORMATION

Rocephin® IV-IM
CEFTRIAXONE SODIUM

Sterile Ceftriaxone Sodium
For Injection
Therapeutic Classification
Antibiotic

INDICATIONS AND CLINICAL USES The treatment of the following infections when caused by susceptible strains of the designated micro-organisms: **Lower respiratory tract infections** caused by *E. coli, H. influenzae, K. pneumoniae* and species, *Staph. aureus, Strep. pneumoniae* and species (excluding enterococci). **Urinary tract infections (complicated and uncomplicated)** caused by *E. coli, Klebsiella* species, *P. mirabilis* and *P. vulgaris*. **Bacterial septicemia** caused by *E. coli, H. influenzae, K. pneumoniae, Staph. aureus* and *Strep. pneumoniae* (excluding enterococci). **Skin and skin structure infections** caused by *K. pneumoniae* and species, *P. mirabilis, Staph. aureus, Staph. epidermidis* and *Streptococcus* species (excluding enterococci). **Bone and joint infections** caused by *Staph. aureus, Strep. pneumoniae* and *Streptococcus* species (excluding enterococci). **Meningitis** caused by *H. influenzae, N. meningitidis*, and *Strep. pneumoniae*. Rocephin® should not be used for the treatment of meningitis caused by *L. monocytogenes*. **Uncomplicated gonorrhea (cervical/urethral and rectal)** caused by *N. gonorrhoeae* (penicillinase and nonpenicillinase producing strains).

Prophylaxis: The preoperative administration of a single 1 g dose of Rocephin® (sterile ceftriaxone sodium) may reduce the incidence of postoperative infections in patients undergoing vaginal or abdominal hysterectomy, coronary artery bypass surgery, or in patients at risk of infection undergoing biliary tract surgery. If signs of post surgical infection should appear, specimens for culture should be obtained for identification of the causative organism(s) so that the appropriate therapy may be instituted. **CONTRAINDICATIONS** Rocephin® (sterile ceftriaxone sodium) is contraindicated in patients with known allergy to ceftriaxone, other cephalosporins or penicillins. **WARNINGS** Before therapy with Rocephin® (sterile ceftriaxone sodium) is instituted, careful inquiry should be made concerning previous hypersensitivity reactions to ceftriaxone, other cephalosporins, penicillins or other allergens. Rocephin® should only be administered with caution to any patient who has demonstrated any form of allergy particularly to drugs. Serious, and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients receiving cephalosporins. The reactions are more likely to occur in persons with a history of sensitivity to multiple allergens. Rocephin® should be administered with caution to patients with type I hypersensitivity reaction to penicillin. If an allergic reaction occurs, the administration of Rocephin® should be discontinued and appropriate therapy instituted. Pseudomembranous colitis has been reported with the use of Rocephin®, (and with broad-spectrum and other antibiotics). Therefore, it is important to consider its diagnosis in patients administered Rocephin® who develop diarrhea. Treatment with broad-spectrum antibiotics, including Rocephin®, alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis. Mild cases of colitis may respond to drug discontinuation alone. Moderate to severe cases should be managed with fluid, electrolyte, and protein supplementation as indicated. When the colitis is not relieved by discontinuation of Rocephin® administration or when it is severe, consideration should be given to the administration of vancomycin or other suitable therapy. Other possible causes of the colitis should also be considered. Rocephin® therapy should be discontinued in patients who develop signs or symptoms suggestive of gallbladder disease and conservative management considered. The effect of pre-existing gallbladder disease is not known. In a few patients administered Rocephin®, shadows suggesting "sludge" have been detected by sonograms of the gallbladder in those who remained asymptomatic and in those who became symptomatic. This condition appeared to be reversible on discontinuation of Rocephin® therapy. In a few symptomatic patients receiving 4 g of Rocephin® who underwent cholecystectomy, "sludge" containing traces of ceftriaxone was recovered from surgical specimens. Concretions consisting of the precipitated calcium salt of ceftriaxone have been found in the gallbladder bile of dogs and baboons treated with high doses of ceftriaxone. **PRECAUTIONS General** Hypoprothrombinemia and alterations in prothrombin time have occurred rarely in patients treated with Rocephin® (sterile ceftriaxone sodium) (see ADVERSE REACTIONS). Patients with impaired vitamin K synthesis or low vitamin K stores (e.g. chronic hepatic disease and malnutrition) may require monitoring of hematology and coagulation parameters during Rocephin® treatment. Vitamin K administration (10 mg weekly) may be necessary if the prothrombin time is prolonged before or during treatment. Prolonged treatment with Rocephin® may result in overgrowth of non-susceptible organisms and organisms initially sensitive to the drug. If superinfection occurs, appropriate measures should be taken. Rocephin® should be administered with caution to individuals with a history of gastrointestinal disease, particularly colitis. **Renal and Hepatic Impairment** Although transient elevations of BUN and serum creatinine have been observed in clinical studies, there is no other evidence that Rocephin®, when administered alone, is nephrotoxic. In severe renal impairment (creatinine clearance of less than 10 mL/min), periodic monitoring of serum ceftriaxone concentrations is recommended. The maximum daily dose should not exceed 2 g. In severe renal impairment associated with clinically significant hepatic impairment, close monitoring of serum ceftriaxone concentrations, at regular intervals, is recommended. If there is evidence of accumulation, dosage should be decreased accordingly. **Interactions** Interactions between Rocephin® and other drugs have not been fully evaluated. **Pregnancy** The safety of Rocephin® in the treatment of infections during pregnancy has not been established. Rocephin® should only be used during pregnancy if the likely benefit outweighs the potential risk to the fetus and/or the mother. Ceftriaxone has been detected in the umbilical cord blood, amniotic fluid and placenta. **Nursing Mothers** Ceftriaxone is excreted in human milk at low concentrations. The clinical significance of this is unknown; therefore, caution should be exercised when Rocephin® is administered to a nursing mother. **Neonates** The safety of Rocephin® in neonates (birth to one month of age) has not been established. *In vitro* studies have shown that ceftriaxone can displace bilirubin from serum albumin. Caution should be exercised when considering Rocephin® treatment for hyperbilirubinemic neonates especially if premature. **Elderly Patients** The elimination of ceftriaxone may be reduced in elderly patients possibly due to impairment of both renal and hepatic function. **Drug-Laboratory Test Interactions** Ceftriaxone may interfere with urine glucose determinations utilizing the copper-reduction test (CLINITEST), but not utilizing the glucose-oxidase test (DIASTIX or TES-TAPE) **ADVERSE REACTIONS** During clinical trials with Rocephin® (sterile ceftriaxone sodium) the following adverse reactions have been observed: **Clinical Adverse Experiences: Dermatological**: Rash (1.3%); exanthema, allergic dermatitis and pruritis (0.1 - 1.0%). **Hematological**: Anemia (0.1 - 1.0%); auto-immune hemolytic anemia and serum sickness (<0.1%). **Hepatic**: Jaundice, reports (in asymptomatic and symptomatic patients) of ultrasonographic shadows suggesting precipitations in the gallbladder and reports of gallbladder sludge (<0.1%). **Urogenital**: Moniliasis and vaginitis (0.1 - 1.0%). **Gastrointestinal**: Diarrhea (3.3%); nausea, vomiting, dysgeusia and gastric pain (0.1 - 1.0%); abdominal pain, colitis, flatulence, dyspepsia, pseudomembranous colitis and stomatitis (<0.1%). **Neurological**: Dizziness and headache (0.1 - 1.0%); ataxia and paresthesia (<0.1%). **Miscellaneous**: Fever, chills, diaphoresis, malaise, burning tongue, flushing, edema and anaphylactic shock (0.1 - 1.0%); bronchospasm, palpitations and epistaxis (<0.1%). **Local Reactions at Injection Site**: Pain (9.4%), induration and tenderness (1-2%); phlebitic reactions (0.1 - 1.0%); thrombophlebitis (<0.1%). **Laboratory Abnormalities**: **Hematologic**: Eosinophilia (4.6%), thrombocytosis (5.1%), leukopenia (2.0%); neutropenia, lymphophenia, thrombocytopenia, increase or decrease in hematocrit, prolongation of prothrombin time and decrease in hemoglobin (0.1 - 1.0%); leukocytosis, lymphocytosis, monocytosis, basophilia and decrease in prothrombin time (<0.1%). **Hepatic**: Increase in AST (SGOT) (4.0%)[b], ALT (SGPT) (4.8%)[b], increase in alkaline phosphatase (1.0%); increase in bilirubin (0.1 - 1.0%). **Urinary**: Increase in BUN (1.1%)[c]; increase in creatinine, erythrocyturia, proteinuria and presence of casts in urine (0.1 - 1.0%); glycosuria (<0.1%). [b] Incidence is more frequent in patients less than one year old. [c] Incidence is more frequent in patients less than one year old and over 50 years old. **SYMPTOMS AND TREATMENT OF OVERDOSAGE** Ultrasonographic shadows suggesting precipitations in the kidneys accompanied by calcium ceftriaxone precipitate in the urine was observed in one patient dosed with Rocephin® (sterile ceftriaxone sodium) at 10 g/day (2.5 times the maximum recommended dose). No other case of overdosage has been reported to date with Rocephin®. No specific information on symptoms or treatment is available. Excessive serum concentration of ceftriaxone cannot be reduced by hemodialysis or peritoneal dialysis. Treatment should be symptomatic. **DOSAGE AND ADMINISTRATION** Rocephin® (sterile ceftriaxone sodium) may be administered intravenously or intramuscularly after reconstitution. Dosage and route of administration should be determined by the severity of infection, susceptibility of the causative organisms, and condition of the patient. The intravenous route is preferable for patients with septicemia or other severe or life-threatening infections. **DOSAGE Adults**: Moderate and Severe Infections: Total daily I.M. or I.V dose 1 or 2 g daily. The daily dose may be given as 0.5 or 1 g q12h, or 1 or 2 g q24h. There is limited experience with daily doses of 3-4 g administered as a single dose or two equally divided doses. The total daily dose should not exceed 4 g. Uncomplicated Gonorrhea: Single dose of 250 mg I.M. Infants and Children (one month to 12 years of age) Serious Miscellaneous Infections: Total daily I.M. or I.V. dose 50 or 75 mg/kg administered as 25 or 37.5 mg/kg q12h. The total daily dose should not exceed 2 g. If body weight is 50 kg or more the adult dose should be used. Meningitis: Total daily I.M. or I.V. dose - 100 mg/kg administered as 50 mg/kg* q12h. * With or without a loading dose of 75 mg/kg. The total daily dose should not exceed 4 g. With the exception of gonorrhea, which is treated with a single dose, the administration of Rocephin® should be continued for a minimum of 48 to 72 hours after the patient defervesces or after evidence of bacterial eradication has been obtained, usually 4 to 14 days. In bone and joint infections the average duration of treatment during clinical trials was 6 weeks, with a range of 1 to 13 weeks, depending on the severity of the infection. When treating infections caused by beta-hemolytic *Streptococcus*, it is recommended that therapy be continued for at least 10 days. The average duration of therapy for infections associated with beta-hemolytic *Streptococcus* during clinical trials was 2 weeks, with a range of 1 to 5 weeks, depending on the site and severity of the infection. **Prophylaxis (Vaginal or Abdominal Hysterectomy, Coronary Artery Bypass Surgery, Biliary Tract Surgery):** For preoperative use as prophylaxis before vaginal or abdominal hysterectomy, coronary artery bypass surgery, or biliary tract surgery in patients at risk of infection, a single dose of 1 g administered 1/2 to 2 hours before surgery is recommended. **Impairment of Renal and/or Hepatic Function** In patients with mild to moderate renal impairment, changes in the dosage regimen are not required, **provided liver function is intact**. In cases of preterminal renal failure (creatinine clearance less than 10 mL/min), periodic monitoring of serum ceftriaxone concentrations is recommended. The daily dosage should be limited to 2 g or less. In patients with liver damage, there is no need for the dosage to be reduced **provided renal function is intact**. In cases of coexistent renal and clinically significant hepatic insufficiency, close monitoring of serum ceftriaxone concentrations, at regular intervals, is recommended. If there is evidence of accumulation, dosage should be decreased accordingly. **ADMINISTRATION Intramuscular**: The reconstituted solution of Rocephin® should be administered by deep intragluteal injection. It is recommended that not more than 1 g be injected at a single site. Pain on intramuscular injection is usually mild and less frequent when Rocephin® is administered in sterile 1% Lidocaine solution. **Intravenous (bolus) Injection**: The reconstituted solution should be administered over approximately 5 minutes. **Short Intravenous Infusion**: The further diluted intravenous solution should be given over a period of 10 to 15 minutes in infants and children and 20 to 30 minutes in adults. **NOTE**: Rocephin® solution should not be physically mixed with aminoglycoside antibiotics nor administered at the same site because of possible chemical incompatibility.

PHARMACEUTICAL INFORMATION

Reconstitution

For Intramuscular Use

Reconstitute Rocephin® powder with the appropriate diluent:

- Sterile Water for Injection
- Bacteriostatic Water for Injection
- 0.9% Sodium Chloride Injection
- 1% Lidocaine Solution
- 5% Dextrose Injection

Reconstitute as follows:

Reconstitution Table (IM)

Vial Size	Volume to be added to vial mL	Approximate available volume mL	Approximate average concentration g/mL
0.25 g	0.9	1	0.25
0.5 g	1.8	2	0.25
1.0 g	3.6	4	0.25
2.0 g	7.2	8	0.25

Shake well until dissolved.

NOTE: SOLUTIONS PREPARED FOR INTRAMUSCULAR USE OR ANY SOLUTION CONTAINING LIDOCAINE OR BACTERIOSTATIC WATER FOR INJECTION SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

For Intravenous Use

Reconstitute only with Sterile Water for Injection.
Reconstitute as follows:

Reconstitution Table (IV)

Vial Size	Volume to be added to vial mL	Approximate available volume mL	Approximate average concentration g/mL
0.25 g	2.4	2.5	0.1
0.5 g	4.8	5.0	0.1
1.0 g	9.6	10.0	0.1
2.0 g	19.2	20.0	0.1

Shake well until dissolved. The prepared solution may be further diluted to the desired volume with any of the "Solutions for IV Infusion" listed below.

Solutions for IV Infusion

0.9% Sodium Chloride Injection
5% Dextrose Injection
Dextrose and Sodium Chloride Injection
0.9% Sodium Chloride Injection in ADD-VANTAGE (Abbott) flexible diluent container, 50 mL and 100 mL
5% Dextrose Injection in ADD-VANTAGE (Abbott) flexible diluent container, 50 mL and 100 mL.

Pharmacy Bulk Package Reconstitution for Preparation of Intravenous Infusion Solutions

The closure of the pharmacy bulk vial shall be penetrated only one time after reconstitution, using a suitable sterile transfer device or dispensing set which allows measured dispensing for the contents.

Reconstitution Table for Bulk Pharmacy Package

Vial size	Volume to be added to vial mL	Approximate available volume mL	Approximate average concentration g/mL
10 g	95	100.0	0.1

Shake well until dissolved. Withdraw the required amount and dilute with one of the "Solutions for IV Infusion". Any unused solution remaining within a period of 8 hours should be discarded.

Stability of Solutions - Storage

For complete stability and storage information, consult the Product Monograph.

Incompatibility:

Rocephin® should not be physically mixed with other antimicrobial agents.
Rocephin® should not be added to blood products, protein hydrolysates or amino acids.
Rocephin® should not be added to solutions containing calcium.

DOSAGE FORM

Availability:

1.Rocephin® Vials containing sterile powder equivalent to 0.25 g, 1 g and 2 g of ceftriaxone.
2.Rocephin® Vials containing sterile powder equivalent to 1 g and 2 g of ceftriaxone for use only with Abbott Laboratories Limited ADD-VANTAGE (Abbott) 0.9% Sodium Chloride Injection U.S.P. or 5% Dextrose Injection U.S.P. in 50 mL and 100 mL containers.
3.Rocephin® Pharmacy Bulk Vials containing sterile powder equivalent to 10 g ceftriaxone (not for direct administration). *The availability of the pharmacy bulk vial is restricted to hospitals with a recognized intravenous admixture programme.*

Storage:

Rocephin® sterile powder should be stored at a controlled room temperature (between 15° and 30°C) and protected from light.
Product Monograph available on request.

References:

1. Hell K. Chemotherapy 1989;**35**:228-235. **2.** Rocephin® Product Monograph.

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Hoffmann-La Roche Limited
2455 Meadowpine Boulevard
Mississauga, Ontario L5N 6L7

Original Research in Medicine and Chemistry

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Bilateral Central Dislocation of the Hip: a Case Report

Patrick Kinnard, MD, FRCSC; Richard Lirette, MD, FRCSC

Bilateral central dislocation of the hip occurs rarely. The authors report a case in which the patient was treated successfully by one-stage, bilateral, total hip arthroplasty.

Une dislocation centrale simultanée des deux hanches est rare. Les auteurs présentent un cas traité par prothèse de hanches bilatérale en une séance chirurgicale avec un excellent résultat.

Simultaneous bilateral central dislocation of the hip, which occurs rarely, may be caused by electric or convulsive therapy,[1-4] epileptic seizures, convulsions secondary to hyponatremia or low magnesium and calcium levels after parathyroidectomy[5-7] and cerebrovascular accident.[8]

Case Report

A 70-year-old woman was admitted to the Centre Hospitalier de l'Université Laval with pain in both legs following severe convulsions that occurred 2 weeks after she underwent a hysterectomy. The convulsions were caused by hyponatremia, which was induced by inappropriate secretion of the antidiuretic hormone.

Radiography demonstrated bilateral, central, hip dislocation. The pelvic rings were intact on the right side and disrupted on the left.

The severity of the pain, despite bilateral traction, necessitated a one-stage, bilateral, total hip arthroplasty under general anesthesia. After reduction and fixation of the left pelvic ring, a screw-ring acetabular prosthesis and a standard cemented femoral stem were inserted on each side (Fig. 1).

During the 3.5-hour operation blood loss was 850 mL. There were no postoperative complications, and the patient was allowed to walk with crutches, with no weight bearing on the left side for 6 weeks.

Eighteen months after surgery, the patient was able to walk without pain or limp; she occasionally used a cane when she experienced discomfort but had resumed all her preoperative activities.

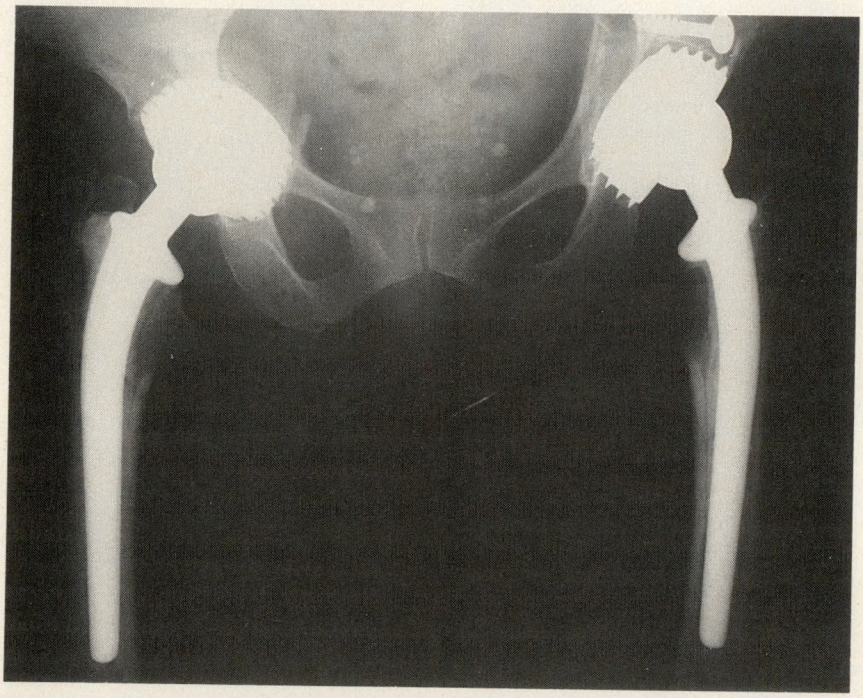

FIG. 1. Pelvis 1 year postoperatively.

Discussion

The mechanism of injury in bilateral central hip dislocation is both complex and controversial.[5,7] It seems likely that the uncontrolled, simultaneous, violent contraction of the pelvitrochanteric muscles generates sufficient force to fracture the acetabular floor and dislocate the femoral head centrally.[5,7] The sym-

From the Department of Surgery, Centre Hospitalier de l'Universitè Laval, Ste. Foy, Que.

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Reprint requests to: Dr. Patrick Kinnard, Professor and head, Division of Orthopedic Surgery, Centre Hospitalier de l'Universitè Laval, 2705 Laurier Blvd., Ste-Foy, PQ G1V 4G2

metric nature of the contractions may account for the bilaterality of the injury.

All patients with this injury reported in the literature were treated by traction and bed rest[2-7] to achieve bone union, which ensued successfully in most cases. If post-traumatic arthritis developed, elective total hip replacement was performed.

In patients with subacute or chronic fracture–dislocation of the hip, a two-stage operation may be preferable, first creating an adequate acetabulum.[9]

For our patient, a one-stage, bilateral, total hip arthroplasty was indicated because she was in severe pain. The one-stage procedure alleviated much of her pain, allowing a more comfortable recovery without complications.

References

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8. PHEN HT, KUMAR NV, IRELAND J: Bilateral central dislocation of the hip following a cerebrovascular accident. *J Bone Joint Surg [Br]* 1989; 71: 703
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Use in Pregnancy

The safety of MEFOXIN® in the treatment of infections during pregnancy has not been established. If the administration of MEFOXIN® during pregnancy is considered necessary, its use requires that the anticipated benefits be weighed against possible hazards to the fetus. Reproductive and teratogenic studies have been performed in mice and rats and have revealed no evidence of impaired fertility or harm to the fetus due to MEFOXIN®.

There are no controlled studies in pregnant women.

Nursing Mothers

Cefoxitin is excreted in human milk. Caution should be exercised if use is indicated.

Children

In children 3 months of age or older, higher doses of MEFOXIN® (100 mg/kg/day and above) have been associated with an increased incidence of eosinophilia and elevated SGOT.

ADVERSE REACTIONS

MEFOXIN® is generally well tolerated. Adverse reactions rarely required cessation of treatment and usually have been mild and transient.

Local Reactions
Thrombophlebitis has occurred with intravenous administration. Some degree of pain and tenderness is usually experienced after intramuscular injections using water. Induration has occasionally been reported.

Allergic
Maculopapular rash, urticaria, pruritus, eosinophilia, fever and other allergic reactions including anaphylaxis have been noted.

Gastrointestinal
Symptoms of pseudomembranous colitis can appear during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Blood
Eosinophilia, leukopenia, neutropenia, hemolytic anemia, and thrombocytopenia and bone marrow depression have been reported. Some individuals, particularly those with azotemia, may develop positive direct Coombs tests during therapy with MEFOXIN®.

Liver Function
Transient elevations in SGOT, SGPT, serum LDH, and serum alkaline phosphatase and jaundice have been reported.

Cardiovascular Function
Hypotension.

Renal Function
Elevations in serum creatinine and/or blood urea nitrogen levels have been observed. As with the cephalosporins, acute renal failure has been reported rarely. The role of MEFOXIN® in changes in renal function tests is difficult to assess, since factors predisposing to prerenal azotemia or to impaired renal function have often been present.

TREATMENT OF OVERDOSE

Other than general supportive treatment, no specific antidote is known. MEFOXIN® can be eliminated by dialysis in patients with renal insufficiency.

DOSAGE AND ADMINISTRATION

MEFOXIN® may be administered intravenously or intramuscularly as required. (See complete monograph on ADMINISTRATION and RECONSTITUTION.)

Intravenous Administration
The intravenous route is preferable for patients with bacteremia, bacterial septicemia, or other severe or life-threatening infections, or for patients who may be poor risks because of lowered resistance resulting from such debilitating conditions as malnutrition, trauma, surgery, diabetes, heart failure, or malignancy, particularly if shock is present or impending.

TREATMENT DOSAGE

Adults

The usual adult dosage is 1 g or 2 g of MEFOXIN® every 6 to 8 hours. Dosage and route of administration should be determined by severity of infection, susceptibility of the causative organisms, and condition of the patient. The usual adult dosages are shown in the Table below.

Usual Adult Dosage

Type of infection	Daily Dosage	Frequency and Route
Uncomplicated forms* of infections such as pneumonia, urinary tract infection, soft tissue infection	3-4 g	1 g every 6-8 h I.V. or I.M.
Moderately severe or severe infections	6-8 g	1 g every 4 h or 2 g every 6-8 h I.V.
Infections commonly needing antibiotics in higher dosage (e.g. gas gangrene)	12 g	2 g every 4 h or 3 g every 6 h I.V.

*Including patients in whom bacteremia is absent or unlikely

Therapy may be started while awaiting the results of susceptibility testing.

Antibiotic therapy for group A beta-hemolytic streptococcal infections should be maintained for at least 10 days to guard against the risk of rheumatic fever or glomerulonephritis. In staphylococcal and other infections involving a collection of pus, surgical drainage should be carried out where indicated.

Adults with Impaired Renal Function

MEFOXIN® may be used in patients with reduced renal function but a reduced dosage should be employed and it is advisable to monitor serum levels in patients with severe impairment.

In adults with renal insufficiency, an initial loading dose of 1 g to 2 g should be given. After a loading dose, the following recommendations for **maintenance dosage** may be used as a guide:

MAINTENANCE DOSAGE OF MEFOXIN® IN ADULTS WITH REDUCED RENAL FUNCTION

RENAL FUNCTION	CREATININE CLEARANCE mL/min	DOSE	FREQUENCY
Mild impairment	50-30	1-2 g	every 8-12 h
Moderate impairment	29-10	1-2 g	every 12-24 h
Severe impairment	9-5	0.5-1 g	every 12-24 h
Essentially no function	<5	0.5-1 g	every 24-48 h

In patients undergoing hemodialysis, the loading dose of 1 - 2 g should be given after each hemodialysis, and the maintenance dose should be given as indicated in the Table above.

Neonates (Including Premature Infants), Infants and Children (See WARNINGS for Neonates under ADMINISTRATION in the complete monograph.)

Premature Infants with Body Weights Above 1500 g	20-40 mg/kg every 12 h I.V.
Neonates	
0-1 week of age	20-40 mg/kg every 12 h I.V.
1-4 weeks of age	20-40 mg/kg every 8 h I.V.
Infants	
1 month to 2 years of age	20-40 mg/kg every 6 h or every 8 h I.M. or I.V.
Children	20-40 mg/kg every 6 h or every 8 h I.M. or I.V.

In severe infections, the total daily dosage in infants and children may be increased to 200 mg/kg, but not to exceed 12 g per day.

MEFOXIN® is not recommended for the therapy of meningitis. If meningitis is suspected, an appropriate antibiotic should be used.

At present there is insufficient data to recommend a specific dosage for children with impaired renal function. However, if the administration of MEFOXIN® is deemed to be essential the dosage should be modified consistent with the recommendations for adults (see Table above).

PROPHYLACTIC USE

For prophylactic use, a three-dose regimen of MEFOXIN® is recommended as follows:

Vaginal or abdominal hysterectomy and abdominal surgery

2 g administered intramuscularly or intravenously just prior to surgery (approximately one-half to one hour before initial incision).

The second and third 2 g doses should be administered at 2-6 hour intervals after the initial dose.

Cesarean Section

The first dose of 2 g should be administered intravenously as soon as the umbilical cord has been clamped. The second and third 2 g doses should be given intravenously or intramuscularly four hours and eight hours after the first dose.

AVAILABILITY

MEFOXIN® is supplied as sterile powder in boxes of 10 vials:

3356 Ca - 1 g cefoxitin as sodium salt
3357 Ca - 2 g cefoxitin as sodium salt
3548 Ca - 1 g cefoxitin as sodium salt in ADD-Vantage® vial
3549 Ca - 2 g cefoxitin as sodium salt in ADD-Vantage® vial

For full details on preparation and administration with ADD-Vantage® vials - please consult Product monograph.

Storage
MEFOXIN® in the dry state should be stored below 30°C. The dry material as well as solutions tends to darken, depending on storage conditions; product potency, however, is not adversely affected.

PRODUCT MONOGRAPH AVAILABLE ON REQUEST

(342-a,11,90)

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MERCK SHARP & DOHME CANADA
P.O. BOX 1005, POINTE-CLAIRE
DORVAL, QUEBEC H9R 4P8

Lymphatic Fistula After Vascular Reconstruction: a Case-Control Study

John L. Murphy, MD, FRCSC; C. William Cole, MD, FRCSC; Prudy M. White, RN; Graeme G. Barber, MD, FRCSC; Adrien G. Bouchard, MD, FRCSC; Neil V. McPhail, MD, FRCSC; Walter G. Waddell, MD, FRCSC, FACS; James L. Wellington, MD, FRCSC, FACS

A retrospective case-control study was carried out to assess the importance of lymphatic fistulas that develop after vascular reconstruction and to determine the risk factors associated with them. The authors compared 35 patients who had lymphatic fistula after vascular reconstruction with 70 control patients, taken from the same database. They found a significant difference between the two groups only in age and indication for surgery: lymphatic fistulas were more likely to develop in older patients and in patients who underwent aortobifemoral bypass for limb salvage rather than for claudication ($p < 0.05$).

Une étude cas-témoins rétrospective a été menée pour établir l'importance des fistules lymphatiques qui surviennent à la suite de reconstructions vasculaires et pour calculer les facteurs de risques qui en découlent. Les auteurs ont comparé 35 patients avec fistules lymphatiques suite à une reconstruction vasculaire avec 70 patients témoins, issus d'une même banque de données. Ils n'ont trouvé de différence significative entre les deux groupes que par rapport à l'âge et l'indication pour la chirurgie: les fistules lymphatiques étaient plus fréquentes chez les patients plus âgés et ceux qui ont subi un contournement aortobifémoral pour récupération d'un membre plutôt que pour claudication ($p < 0.05$).

Lymphatic fistula is an uncommon complication of surgery in the groin but may be of importance in certain circumstances, such as after vascular reconstruction, particularly when prosthetic material is used. Lymphatic fistulas in this situation have been said to heighten the risk of graft infection,[1] but, to our knowledge, this hypothesis has not been tested. The purpose of our study was to assess the importance of lymphatic fistulas occurring after vascular reconstruction and to determine the risk factors associated with them.

Methods

Review of a computerized database of vascular surgery patients treated at the Ottawa Civic and Ottawa General hospitals between 1982 and 1987 was used to identify those with lymphatic fistula, defined in this study as clear, watery drainage from a groin wound that was present 7 or more days postoperatively. A control group was selected from the same database by taking the nearest numbered record of a patient with a groin wound before and after each case of lymphatic fistula. The majority of study subjects were interviewed and examined by one of us (J.L.M.), and additional information was obtained by a review of the hospital records. Data were analysed by comparison of the two groups using the χ^2 test with Yates' correction and Student's *t*-test when required.

Findings

Thirty-five patients satisfied the criteria for inclusion in the study. The demographic characteristics of the two groups were comparable. Patients with a lymphatic fistula differed from control patients in two important variables: age and indication for surgery. Those with a lymphatic fistula were older (Table I) and had undergone surgery more often for limb salvage than for claudication (Table II).

Throughout the follow-up there were no graft infections or pseudo-

From the Division of Vascular Surgery, Department of Surgery, Ottawa Civic Hospital, Ottawa

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Reprint requests to: Dr. C. William Cole, Division of Vascular Surgery, Ottawa Civic Hospital, 1053 Carling Ave., Ottawa, ON K1Y 4E9

aneurysms in either group (Table III). During that time two graft occlusions occurred in the fistula group and six among the controls. The causes of death in the fistula group included myocardial infarction (four patients), carcinoma (four), stroke (three) and others (three); no death was attributed to a graft complication. Other factors that may have influenced wound healing and perhaps contributed to the development of a lymphatic fistula were diabetes (seven patients), renal failure (two), steroid therapy (two) and repeat surgery that involved a previous groin incision (six).

Cultures of the lymphatic drainage were positive in 8 of the 35 patients with a lymphatic fistula (Table IV). However, only two had clinically apparent superficial wound infections; one infection developed after a lymphocele was aspirated. These infections resolved with intravenous antibiotic therapy, and there were no long-term sequelae.

Drainage from the fistula persisted for an average of 28 days and resulted in prolonged hospital stay in most cases, but no other problems arose over a follow-up that averaged more than 3 years. The management of all cases consisted of bed rest and scrupulous wound care together with continuous antibiotic therapy; none had surgical exploration.

Table I. Demographic Characteristics of 35 Patients With Lymphatic Fistula and 70 Control Patients

	Group		
Patients	**Fistula**	**Control**	***p* value**
Mean age, yr	69.9	63.4	< 0.05*
Sex, M:F	31:4	51:19	NS
Smokers, no.	31	57	NS
Diabetics, no.	7 (all men)	14	NS

*Two-tailed Student's *t*-test.

Table II. Indication for Operation and Type of Reconstruction

	Group		
Indication/procedure	**Fistula**	**Control**	***p* value**
Aneurysm			NS
Aortobifemoral bypass	13	14	
Occlusive disease			< 0.01*
Claudication			
Aortobifemoral bypass	2	24	
Limb salvage†			
Aortobifemoral bypass	4	32	
Femorofemoral bypass	1	—	
Femoropopliteal bypass	8	—	
Femorotibial bypass	2	—	
Axillofemoral bypass	5	—	
Other	1	—	

*χ^2 with Yates' correction.
†One patient had aortobifemoral and femoropopliteal bypass.

Table III. Outcome Over 5 Years

	Group	
Outcome	**Fistula**	**Control**
Follow-up, mo		
Mean	42.7	41.5
Range	6–84	12–84
Positive culture, no.	8	1
Superficial infection, no.	2	2
Graft infection, no.	0	0
Anastomotic aneurysm, no.	0	0
Graft occlusion, no.	2	6
Death, no.	14	10
Lost to follow-up, no.	5	14

Discussion

The findings from this study show that lymphatic fistulas complicating vascular reconstructive surgery in the groin do not frequently lead to graft infection. The importance of a postoperative lymphatic fistula in this group of patients may therefore depend upon other factors. It has been suggested that distal foot lesions may allow microorganisms to be transported to the groin by way of lymph channels, with resultant local contamination and infection in a prosthetic graft.[2] Graft infection was not seen in this series, but the significance of distal foot lesions can be appreciated when 20 of the 22 patients with occlusive disease had limb-threatening ischemia compared with 32 of the 56 control patients with occlusive disease ($p < 0.01$). The type of reconstruction may also be a factor in the development of a lymphatic fistula: none of the control patients in this study had popliteal or tibial incisions compared with 10 patients

Table IV. Microorganisms Isolated From the Groin of Eight Patients With Lymphatic Fistula

Organism isolated	**Number of isolates**
Staphylococcus epidermidis	4
Pseudomonas aeruginosa	2
Enterococcus	3
Staphylococcus aureus	2
Escherichia coli	2
Mixed organisms	3

with lymphatic fistula (Table II). When taken together, these data suggest that distal procedures associated with severe ischemic changes are more likely to result in a lymphatic fistula at the groin than bypasses to the femoral artery for proximal occlusive disease.

The incidence of lymphatic fistula reported in the literature is inconsistent and often not accompanied by a clear definition of what is meant by the term. In many groin wounds lymph drainage occurs for a short time and is not always reported. In a recent multicentre, prospective study of aneurysm surgery only three lymphatic fistulas were noted in 367 groin anastomoses.[3] This may represent underreporting since another report of 423 groin wounds identified 27 cases of lymphatic fistula.[4] In that report, only 9 of 22 patients had lymph drainage for more than 5 days.[4] There is no widely accepted definition of a lymphatic fistula and little more agreement regarding its importance. When clear lymph drainage is abundant or when drainage persists beyond the usual time for a patient to be discharged from hospital, most would agree that a lymphatic fistula exists. The present study included only fistulas that were present 7 or more days postoperatively, to distinguish them from minor wound drainage that may moisten a groin dressing in the early postoperative period.

The management of lymphatic fistula is the subject of considerable controversy. All patients in this series were treated nonoperatively, but others have recommended a more aggressive, surgical approach. Kwaan, Bernstein and Connolly[5] compared operative and nonoperative management in a small series. On the basis of one graft infection in seven nonoperative cases compared with none in five managed surgically, they concluded that operative treatment reduced hospital stay and the risk of graft infection. The present series is larger and the follow-up longer. Our findings support a contrary position: that nonoperative therapy has a low incidence of infectious complications and most fistulas will respond without operative intervention. Surgery may be required for fistulas draining very large volumes of lymph or those that fail to respond to nonoperative management. The nature of the microorganisms present in a groin wound infection largely determines the consequences. Arteries infected with *Staphylococcus aureus* or gram-negative organisms, or both, more often result in disruption than arteries infected with *Staphylococcus epidermidis*.[6] The organisms cultured from the draining lymph in the cases reported here were more often *S. epidermidis* than any other. It is possible that greater contamination with a more virulent organism such as *Pseudomonas* sp. would have resulted in a much different outcome. No correlation was noted between culture results and the presence of open or infected foot lesions. However, the observation that a lymphatic fistula occurred more often in patients operated upon for limb salvage may be of more than passing importance. Many patients with severe ischemia present with edema in the affected part, which is due mainly to two causes: first, with severe ischemia patients keep the limb in a position of dependency, even at rest, which results in clinically apparent edema; second, ischemic tissues lose the integrity of cell membranes and leak fluid into the interstitium. Postoperatively, this results in a greater volume of lymph flow through channels in the groin that have a reduced capacity as a result of the surgical procedure.

Important risk factors predisposing to the development of a lymphatic fistula in the groin were advanced age and surgery for limb salvage. A consequence of this complication was prolonged hospital stay, but the clinical course and outcome were not otherwise influenced.

We thank David Moher, Department of Research, for statistical support and assistance with study design, and Lise Fournier for follow-up of patients.

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ATLAS OF ORTHOPAEDIC PATHOLOGY. Lester E. Wold, Richard A. McLeod, Franklin H. Sim et al. Atlases in Diagnostic Surgical Pathology series; editor, Gerald M. Bordin. 276 pp. Illust. W.B. Saunders Company, London/Harcourt Brace Jovanovich, Inc., Philadelphia; HBJ-Holt-Saunders Distribution Services, Toronto. 1990. Price not stated. ISBN 0-7216-2911-3

This atlas is one of a proposed series relating to specific, well-defined areas of specialty pathology. It has been prepared by four staff members of the Mayo Clinic — two pathologists, a radiologist and an orthopedic surgeon who has a specific interest in orthopedic oncology.

The book is well organized into seven sections, each section being clearly defined by the common factor of the cell or origin of the lesions to be discussed. Thus, section one is on osteoid-forming lesions, section two on cartilage-forming lesions, section three on fibrous lesions, and so on. This allows for a speedy reference to lesions of similar origin. Each tumour or tumour-like condition within each section is given a short chapter, which begins with a brief discussion of the incidence of the lesion, signs and symptoms, major radiographic features, differential diagnosis and the histology. The introduction is followed by lavishly illustrated examples of the gross and microscopic appearances, including radiographs and some clinical photographs. The illustrations are superb.

This textbook sets out admirably to accomplish its goal. For the practising surgeon, it is an excellent reference for the pathologic features of malignant and benign musculoskeletal tumours. Unfortunately, it is restricted in its scope to tumour pathology, so that many important pathological conditions affecting the musculoskeletal system are ignored. The text therefore is misnamed — it is not an atlas of orthopedic pathology but an atlas of tumours and tumour-like conditions of bone and connective tissue.

Despite this shortcoming it remains an excellent reference text for practising surgeons and surgical trainees. It will prove invaluable for orthopedic surgeons in training in improving their understanding and knowledge of these relatively uncommon conditions and will greatly assist them in formulating differential diagnoses based upon the clinical and radiographic presentation of these lesions.

James P. Waddell, MD, FRCSC
Surgeon-in-chief
Division of Orthopedics
St. Michael's Hospital
Toronto, ON
M5B 1W8

METABOLIC BONE DISEASE AND CLINICALLY RELATED DISORDERS. 2nd ed. Edited by Louis V. Avioli and Stephen M. Krane. 912 pp. Illust. W.B. Saunders Co./Harcourt Brace Jovanovich, Inc. Philadelphia. 1990. $240. ISBN 0-7216-2766-8

Readers should first be aware that the reviewer of this book is an orthopedic surgeon: this review is therefore from the point of view of an orthopedic surgeon, and a senior one at that.

This text first appeared in two volumes in 1977 and 1979. This second edition, now one volume, attempts "to present a correlated view of metabolic bone disease and related topics, stressing the relationship between genetics, molecular biology, biochemistry, pathology, and clinical syndromes, in a single volume." The editors appear to have accomplished their goals by producing a relatively compact book of just under 1000 pages which, nevertheless, covers a frequently poorly understood group of bone diseases, including osteopetrosis, osteogenesis imperfecta, Gaucher's disease and sarcoidosis, as well as female osteoporosis syndrome, osteomalacia, renal osteodystrophy and hyperparathyroidism. A chapter on metabolic bone disorders in children is a welcome addition, and one on tumours of bone is perhaps justified, at least on the basis of differential diagnosis.

The editors are professors of medicine, in St. Louis and Boston respectively, and they have put together contributions from 40 authors, almost exclusively North American. Interestingly, the only "foreign" authors are from Melbourne, Australia, and they have contributed the chapter on a Canadian discovery, calcitonin.

Two features are immediately evident: the relative paucity of illustrations (which presages a large amount of solid reading) and the very extensive reference lists for each chapter. A quick check for the *least* number of references revealed the chapter on hypercalcemia of malignant disease (a useful one for orthopedic surgeons) with 87; several chapters contain over 500 references.

The index was put to the test on a number of occasions and responded consistently and with ease. Subjects dear to the hearts of orthopedic surgeons (alkaline phosphatase, myositis ossificans, fractures in Paget's disease) were easily traced.

As a clinician, I found it difficult to adjust to the scientific terminology (dare I say jargon?), but after a chapter or two it came with greater ease. As a reader of English, I also had occasional difficulty with words. "Solubilization" tied my silent tongue, but it is in Webster's dictionary.

The book, therefore, is judged to be an extensive compilation of current knowledge in its field, and as such should be a useful reference for those physicians and surgeons clinically active in the area of skeletal diseases and injuries. Its subtitle "and Clinically Related Disorders" is significant. It is not simply a large tome on osteoporosis with a number of exotic but rare diseases added. It includes conditions encountered daily in orthopedic practice and is broadened by inclusion of a wide group of conditions as differential diagnoses.

At the list price of $240 it is unlikely to grace the shelves of many personal libraries but should be an essential addition to all group-practice and medical-centre libraries.

Kenneth S. Morton, MD, CM, FRCSC
Department of Orthopedics
3rd Floor
910 W 10th Ave.
Vancouver, BC
V5Z 4E3

SHOULDER RECONSTRUCTION. Charles S. Neer II. Illustrated by Robert J. Demarest. 551 pp. Illust. W.B. Saunders Company, London/Harcourt Brace Jovanovich, Inc., Philadelphia; HBJ-Holt-Saunders Distribution Services, Toronto. 1990. $165. ISBN 0-7216-2832-X

Shoulder surgery has attracted the interest of many orthopedic surgeons and allied health professionals in the last decade. Before then, this joint was rarely the focus of any major discussion, and surgical treatment was offered by only a few who had special interest in that area. Dr. Neer became interested in this joint early in his career. Stimulated by his teacher, Dr. Harrison McLaughlin, Neer makes his vast experience available to the reader in this extensive book. In it he combines an underlying pathologic condition with a clear indication for a procedure and details the potential pitfalls.

The figures by Robert J. Demarest are of high quality and vividly illustrate Neer's concepts from his earlier, well-known articles. The figures are accompanied by detailed anatomic drawings and radiographs, outlining the individual pathologic conditions.

The anatomy of the shoulder region and related conditions are described in detail. A chapter on shoulder rehabilitation will be of interest to the orthopedic surgeon and to all personnel involved in restoring shoulder-girdle function.

The remaining five chapters focus on all the common shoulder disorders. Cuff lesions and impingements as well as glenohumeral arthroplasty are covered, reflecting the author's long-time interests. The chapter on fractures of the shoulder clearly outlines the pathologic concept and eventual outcome of any fracture and its treatment. Neer deserves the credit for creating a classification that has become the common knowledge base for the treatment of shoulder fractures.

An extensive collection of references reflects the volume of Neer's work and will direct orthopedic surgeons to additional topics of interest.

This book is a pleasure to read and a necessity for any orthopedic surgeon working in this field. Its clear concept and excellent illustrations make it very attractive for professionals in related specialties such as rheumatology and physical medicine.

Joachim F. Lohr, MD, FRCSC
Assistant professor of surgery,
University of Ottawa,
Ottawa General Hospital,
Ottawa, ON
K1H 8L6

NOTICES

Congrès annuel de l'Association des chirurgiens généreux du Québec

L'Association des chirurgiens généreux du Québec tiendra son congrès annuel les jeudi et vendredi, 2 et 3 mai 1991 chez le Château Frontenac, Québec. Pour renseignements s'adresser au secrétariat de l'Association: (514) 393-9179.

Laparoscopic Cholecystectomy

The Department of Surgery, University of Toronto, will be holding postgraduate courses in laparoscopic cholecystectomy for general surgeons, at the Mount Sinai Hospital, Toronto, on the following dates: Mar. 20 and 21, 1991; Apr. 3 and 4, 1991; Apr. 17 and 18, 1991; May 1 and 2, 1991; May 15 and 16, 1991; May 29 and 30, 1991 and June 26 and 27, 1991. (These dates may be subject to change.) For further information please contact: Dr. S.M. Strasberg, Course director, Mount Sinai Hospital, Rm. 1225, 600 University Ave., Toronto, ON M5G 1X5; phone: (416) 586-8420; fax: (416) 586-8392.

Gastrointestinal Surgery for Severe Obesity

A National Institutes of Health Consensus Development Conference on gastrointestinal surgery for severe obesity will be held from Mar. 25 to 27, 1991 in the Masur Auditorium, The Warren Grant Magnuson Clinical Center, National Institutes of Health, Bethesda, Md. For further information contact: Conference registrar, Prospect Associates, 1801 Rockville Pike, Ste. 500, Rockville, MD 20852; phone: (301) 468-MEET; fax: (301) 770-5164.

Only three patients had to be discontinued from therapy because of laboratory adverse experiences, however laboratory abnormalities were present at baseline.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

There is no experience to date with deliberate overdosage. Doses of up to 640 mg/day have been employed in patients with pathological hypersecretory conditions with no serious adverse effects. In the event of overdosage, treatment should be symptomatic and supportive. Unabsorbed material should be removed from the gastrointestinal tract, the patient should be monitored, and supportive therapy should be employed.

The oral LD_{50} of famotidine in male and female rats and mice was >5000 mg/kg.

DOSAGE AND ADMINISTRATION

DUODENAL ULCER

Acute Therapy
The recommended adult oral dosage of PEPCID® (famotidine) for acute duodenal ulcer is 40 mg once a day at bedtime. Treatment should be given for 4-8 weeks, but the duration of treatment may be shortened if healing can be documented. Healing occurs within 4 weeks in most cases of duodenal ulcer.

Maintenance Therapy
For the prevention of recurrence of duodenal ulcer, it is recommended that therapy with PEPCID® be continued with a dose of 20 mg once a day at bedtime, for a duration of up to 6-12 months depending on the severity of the condition.

BENIGN GASTRIC ULCER

Acute Therapy
The recommended adult oral dosage for acute benign gastric ulcer is 40 mg once a day at bedtime. Treatment should be given for 4 to 8 weeks, but the duration of treatment may be shortened if healing can be documented.

PATHOLOGICAL HYPERSECRETORY CONDITIONS (SUCH AS ZOLLINGER-ELLISON SYNDROME)

The dosage of PEPCID® in patients with pathological hypersecretory conditions varies with the individual patient. The recommended adult oral starting dose for pathological hypersecretory conditions is 20 mg q6h. In some patients, a higher starting dose may be required.

Doses should be adjusted to individual patient needs and should continue as long as clinically indicated. Doses up to 160 mg q6h have been administered to some patients with severe Zollinger-Ellison syndrome.

Intravenous Administration
In some hospitalized patients with pathological hypersecretory conditions or intractable ulcers, or in patients who are unable to take oral medication, PEPCID® I.V. may be administered. The recommended dosage is 20 mg every 12 hours.

Intravenous injection therapy should be changed to oral treatment as soon as the acute situation is under control.

Concomitant Use with Antacids
Antacids may be given concomitantly if needed.

Dosage Adjustment for Patients with Severe Renal Insufficiency
In patients with advanced renal insufficiency, i.e., with a creatinine clearance less than 10 mL/min., the elimination half-life of PEPCID® may exceed 12 hours reaching approximately 24 hours in anuric patients.

To avoid excess accumulation of the drug, the dosing interval of PEPCID® may be prolonged to 36-48 hours as indicated by the patient's clinical response.

PHARMACEUTICAL INFORMATION

COMPOSITION

Tablets
Each tablet for oral administration contains either 20 mg or 40 mg of famotidine.

Injection
Each mL of the solution for intravenous injection contains 10 mg of famotidine and the following inactive ingredients: L-aspartic acid 4 mg, mannitol 20 mg, and Water for Injection, q.s., 1 mL. The multidose injection also contains benzyl alcohol 0.9% added as preservative.

RECONSTITUTION

Parenteral Products

Dilution of PEPCID® I.V. for Infusion

PEPCID® I.V. Solution	Vol.....e of Compatible I.V. Solution	Final Volume	Final Concentration	Rate of Infusion
2 mL	3 mL	5 mL	4 mg/mL	Not less than 2 minutes
2 mL	8 mL	10 mL	2 mg/mL	Not less than 2 minutes
2 mL	100 mL	102 mL	0.196 mg/mL	15-30 minutes

PEPCID® I.V. Solutions are compatible with:

Water for Injection
0.9% Sodium Chloride Injection
5% Dextrose Injection
10% Dextrose Injection
Lactated Ringer's Injection
Sodium Bicarbonate Injection 5%

STABILITY AND STORAGE RECOMMENDATIONS

PEPCID® I.V. Solution
Store at 2 - 8°C. Protect from light. If solution freezes, bring the solution to room temperature; allow sufficient time to solubilize all the components.

Diluted PEPCID® I.V. Solutions should be used within 24 hours due to the possibility of microbial contamination during preparation.

NOTE: Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit.

DOSAGE FORMS AND AVAILABILITY

Tablets PEPCID® (famotidine tablets) are D-shaped, film-coated tablets supplied as follows:

No. Ca 8102 - 20 mg beige coloured, coded 963. Available in bottles of 100 tablets.

No. Ca 8103 - 40 mg light brownish orange, coded 964. Available in bottles of 100 tablets.

No. Ca 3539 - PEPCID® I.V., 10 mg per 1 mL, is a clear, colourless solution and is available as a non-preserved unit dose containing 2 mL of injectable solution. Available in 10 x 2 mL vials.

No. Ca 3541 - PEPCID® I.V., 10 mg per 1 mL, is a clear, colourless solution and is available as a preserved multiple dose containing 4 mL of injectable solution. Available in 4 mL vials.

HUMAN PHARMACOLOGY

In both normal volunteers and hypersecretors, PEPCID® inhibited basal nocturnal and daytime gastric secretion, as well as secretion stimulated by a variety of stimuli, such as pentagastrin and food.

After oral administration, the onset of the antisecretory effect occurred within one hour; the maximum effect was dose-dependent, occurring within one to three hours. Duration of inhibition of secretion was 10 to 12 hours. After intravenous administration, the maximum effect was achieved within 30 minutes. Single intravenous doses of 10 and 20 mg inhibited basal nocturnal secretion for a period of 10-12 hours. The 20 mg dose was associated with the longest duration of action in most subjects. Single oral doses of 20 and 40 mg inhibited basal nocturnal acid secretion in all subjects; mean gastric acid secretion was inhibited by 86% and 94%, respectively, for a period of at least 10 hours. Similar doses given in the morning suppressed food-stimulated acid secretion in all subjects, with mean suppression of 76% and 84%, respectively, 3 to 5 hours after drug, and of 25% and 30%, respectively, 8 to 10 hours after drug; however, in some subjects who received the 20 mg dose, the antisecretory effect was dissipated earlier, within 6-8 hours. There was no cumulative effect with repeated doses. The basal nocturnal intragastric pH was raised by evening doses of 20 and 40 mg of PEPCID® to mean values of 5.0 and 6.4, respectively. When PEPCID® was given in the morning, the basal daytime interdigestive pH at 3 and 8 hours after 20 or 40 mg of PEPCID® was raised to about 5.0.

Fasting and postprandial serum gastrin levels may be slightly elevated during periods of drug antisecretory effect, and with chronic therapy an increase in gastric bacterial flora may occur. Gastric emptying and exocrine pancreatic function are not affected by PEPCID®.

Other effects
Systemic pharmacologic effects of PEPCID® in the CNS, cardiovascular, respiratory or endocrine systems have not been found to date. Serum prolactin levels do not rise after intravenous bolus doses of 20 mg PEPCID® and no antiandrogenic effects have been detected.

Pharmacokinetics
PEPCID® is incompletely absorbed. The bioavailability of oral doses is 40-45%. Bioavailability may be slightly increased by food, or slightly decreased by acntacids; however, these effects are of no clinical consequence. PEPCID® undergoes minimal first-pass metabolism. After oral doses, peak plasma levels occur in 1-3 hours. Plasma levels after multiple doses are similar to those after single doses. Fifteen to 20% of PEPCID® in plasma is protein bound. PEPCID® has an elimination half-life of 2.5-3.5 hours. PEPCID® is eliminated by renal (65-70%) and metabolic (30-35%) routes. Renal clearance is 250-450 mL/min., indicating some tubular excretion.

Twenty-five to 30% of an oral dose and 65-70% of an intravenous dose are recovered in the urine as unchanged compound. The only metabolite identified in man is the S-oxide. There is a close relationship between creatinine clearance values and the elimination half-life of PEPCID®. In patients with severe renal insufficiency, i.e., creatinine clearance less than 10 mL/min., PEPCID® elimination half-life may exceed 20 hours and adjustment of dosing intervals may be necessary (see PRECAUTIONS, DOSAGE AND ADMINISTRATION). In elderly patients, there are no clinically significant age-related changes in the pharmacokinetics of PEPCID®.

PRODUCT MONOGRAPH AVAILABLE ON REQUEST

(320-a,9,87)

References for ads PCD-90-3105-JA, PCD-90-3106-JA and PCD-90-3391-JA

1. Bianchi Porro, G. et al.: Review of an extensive worldwide study of a new H_2-receptor antagonist, famotidine, as compared to ranitidine in the treatment of acute duodenal ulcer, J Clin Gastroenterol **9(suppl 2)**:14-18, 1987.
2. Savarino, V. et al.: Continuous 24-hour intragastric pH monitoring in the evaluation of the effect of a nightly dose of famotidine, ranitidine and placebo on gastric acidity of patients with duodenal ulcer, Digestion, **37**:103-109, 1987.
3. Schunack, W.: What are the differences between the H_2-receptor antagonists? Aliment Pharmacol Therap, **1**:493S-503S, 1987.
4. Texter, E.C. et al.: Maintenance therapy of duodenal ulcer with famotidine. A multicenter United States study, Am J Med, **81(suppl 4B)**: 20-27, Oct 1986.

Reference for ad PCD-90-3392-JA

1. Texter, E.C. et al.: Maintenance therapy of duodenal ulcer with famotidine. A multicenter United States study, Am J Med, **81(suppl 4B)**: 20-27, Oct 1986.

Reference for ad PCD-90-3103-JA

1. Ryan, J.R. et al.: Comparison of effects of oral and intravenous famotidine on inhibition of nocturnal gastric acid secretion, Am J Med, **81(suppl 4B)**:60-64. Oct 1986.

3105/3106/3391/3392/3103

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Box replies should be addressed as follows: Box ---, *Canadian Journal of Surgery*, PO Box 8650, Ottawa, Ontario K1G 0G8.

University of Ottawa—Faculty of Medicine
Chair of the University Division of General Surgery

The University of Ottawa invites applications for the position of Chairperson of the University Division of General Surgery.

Applicants must be eligible to practise in Ontario and hold certification of the Royal College of Physicians and Surgeons of Canada in general surgery. The faculty is seeking an individual with a track record of clinical and academic excellence, leadership skills and potential to develop a strong research program in general surgery.

The division is responsible for directing both undergraduate teaching and postgraduate programs in general surgery in the Ottawa Civic Hospital and Ottawa General Hospital and Children's Hospital of Eastern Ontario. The successful candidate will hold a joint appointment as Chair of the University Department of General Surgery and Head at one of the affiliated teaching hospitals.

The faculty is seeking an individual who will hold a full-time University appointment. Salary and fringe benefits are commensurate with qualifications and experience, and are in accordance with existing scales at the University of Ottawa.

Priority will be given to Canadian citizens and permanent residents of Canada in accordance with Canadian immigration requirements. Employment equity is university policy.

A working knowledge of both English and French is desirable and a commitment to support bilingualism within the faculty is essential.

Applicants are requested to forward their curriculum vitae and the names of three referees prior to May 15, 1991.

John F. Seely, MD.
Dean, Faculty of Medicine
University of Ottawa
451 Smyth Road
Ottawa, Ontario
K1H 8M5

Université d'Ottawa — Faculté de médecine
Chaire de la division universitaire de chirurgie générale

L'Université d'Ottawa accueille les candidatures à la direction de sa chaire de chirurgie générale.

Les candidats et candidates doivent être admissibles à exercer la profession en Ontario et posséder l'agrément à titre de spécialiste du Collège royal des médecins et chirurgiens du Canada, tout en faisant preuve de réalisations et d'expérience en chirurgie générale clinique et universitaire. Le poste comporte un rôle de direction dans les milieux universitaire, hospitalier et communautaire et la préférence sera accordée à une personne compétente qui s'est engagée dans la voie de l'excellence universitaire en enseignement et en recherche.

La division à la responsabilité de fournir un enseignement de qualité au niveau prédiplomé et postdoctoral dans les hôpitaux affiliés offrant une formation en chirurgie générale soit l'Hôpital Civic d'Ottawa, l'Hôpital Général d'Ottawa et l'Hôpital pour enfants de l'Est de l'Ontario. La personne retenue assumera une double affectation à la direction de la chaire de chirurgie générale de l'université et à la direction de chirurgie générale dans un des hôpitaux d'enseignement mentionnés.

La faculté est à la recherche d'une personne pour combler un poste à temps complet. Le traitement et les avantages sont fonction de la formation et de l'expérience, conformément à l'échelle en vigueur à l'Université d'Ottawa.

En vertu des exigences canadiennes relatives à l'immigration, la priorité est accordée aux personnes de citoyenneté canadienne et de résidence permanente au Canada. L'université a une politique d'égalité en matière d'emploi.

Une connaissance de l'anglais et du francais est désirable. Un engagement à promouvoir le bilinguisme au sein de la faculté est essentiel.

Prière d'envoyer les demandes, accompagnées d'un curriculum vitae et du nom de trois répondants, à l'adresse ci-dessous avant le 15 mai 1991.

John F. Seely, MD
Doyen, Faculté de médecine
Université d'Ottawa
451, chemin Smyth
Ottawa (Ontario)
K1H 8M5

S91-47

The Department of Surgery
University of Toronto

announces

Post Graduate Courses
in Laparoscopic Cholecystectomy
for General Surgeons

The courses are scheduled between January and June 1991 and will be two days in duration. They will involve theoretical and practical sessions in the surgical laboratory and in the operating room.

For further information write or call:
Dr. Steven M. Strasberg - Course Director
Mount Sinai Hospital
Room 1225
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Fax: (416) 586-8392
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S91-42

FELLOWSHIP, CARDIOPULMONARY TRANSPLANTATION: ON – Busy heart, heart-lung and lung transplant centre performing 45-50 transplants a year requires a board eligible/certified thoracic surgeon to work as a transplant fellow commencing July 1991. Responsibilities will include donor and recipient operations, postoperative care and participating in ongoing experimental and clinical research protocols. Contact: **Dr. Neil McKenzie, University Hospital, PO Box 5339, London, ON N6A 5A5.** –S91-46

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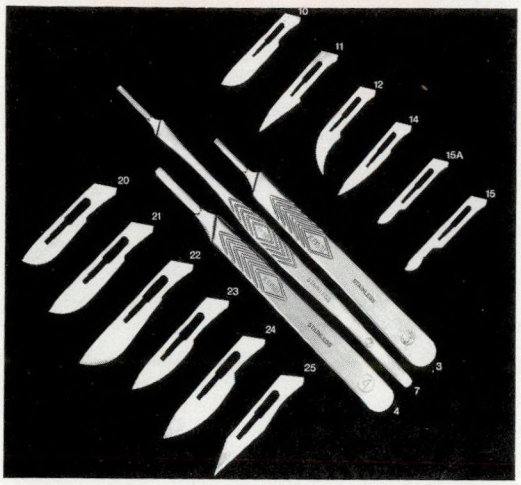

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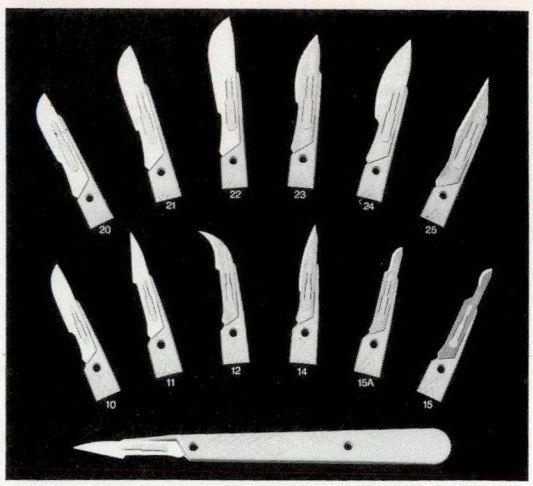

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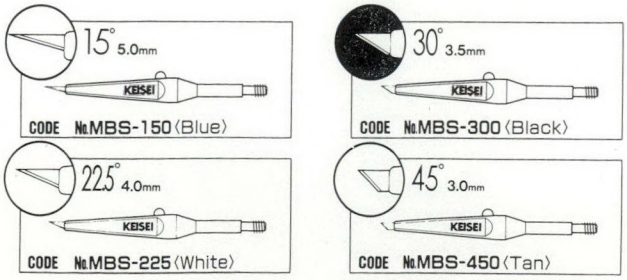

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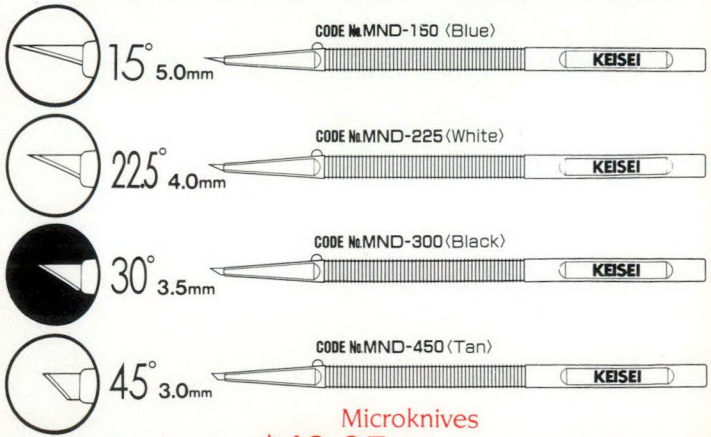

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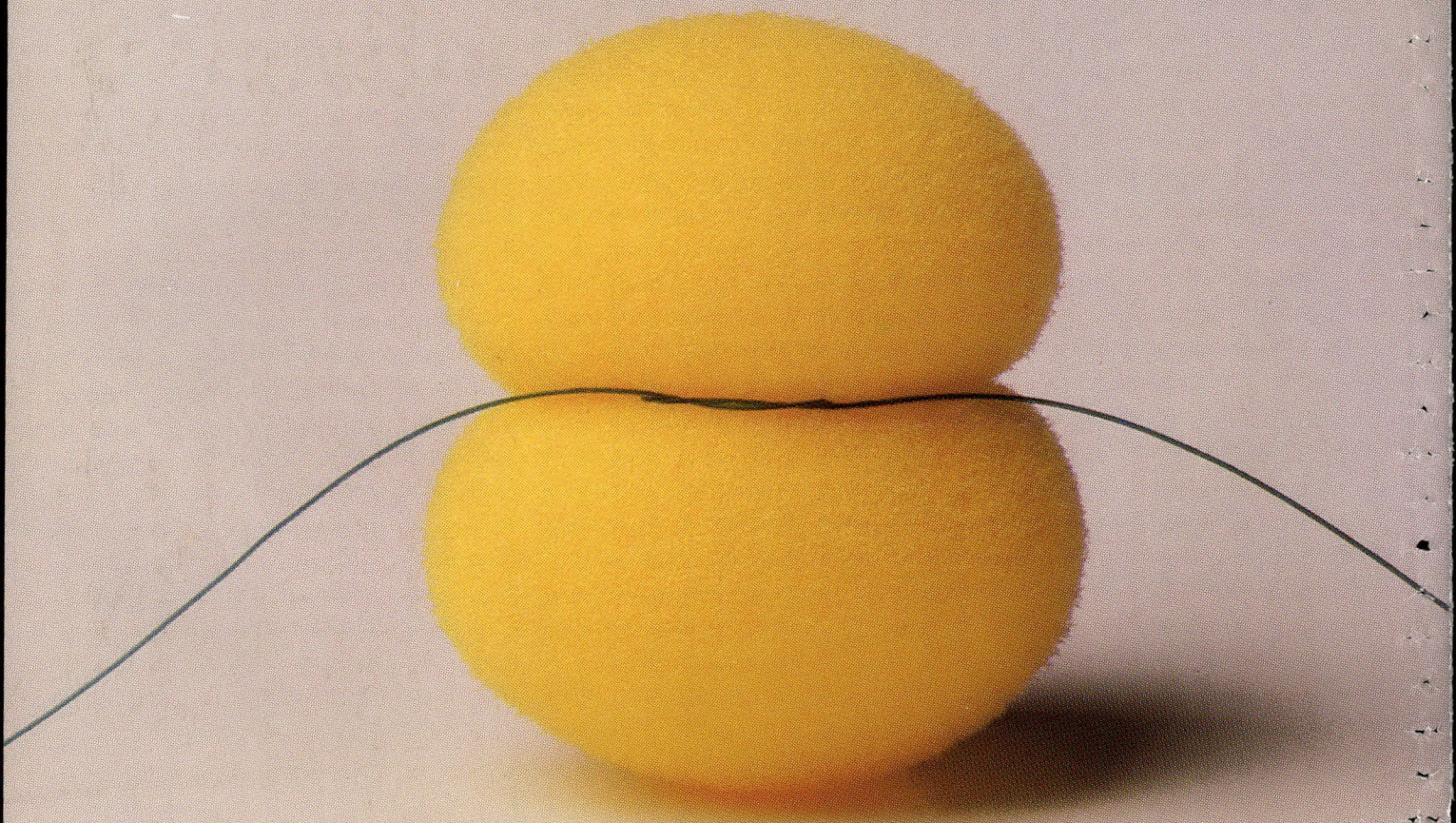

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